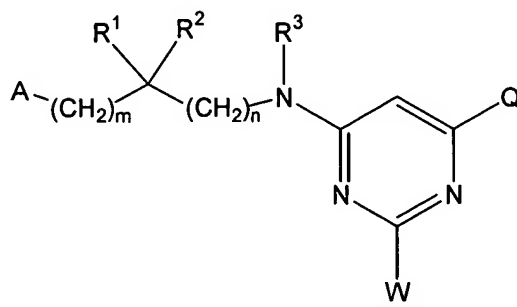


# CLAIM AMENDMENTS

1-3. (canceled)

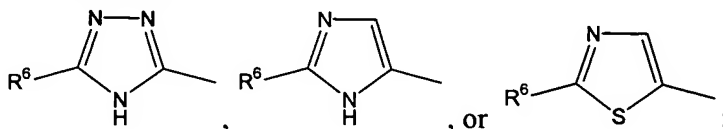
4. (currently amended) ~~A 4-pyrimidineamine according to claim 3 wherein~~ A compound of formula



wherein:

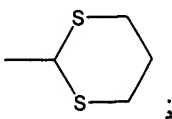
A is A<sup>1</sup> or A<sup>2</sup>;

A<sup>1</sup> is R<sup>4</sup>R<sup>5</sup>N-C(O)-;



A<sup>2</sup> is chosen from R<sup>7</sup>C(O)NH-, R<sup>7</sup>S(O)<sub>2</sub>NH-, R<sup>4</sup>NH-, and R<sup>4</sup>O-;

Q is chosen from imidazolyl, methylimidazolyl, pyrrolyl, methylpyrrolyl, pyrazolyl, methylpyrazolyl, hydroxymethylimidazolyl, (dimethylaminomethyl)imidazolyl, furanyl, methylfuranyl, thienyl, oxazolyl, thiazolyl, pyridinyl, quinolinyl, 1-methylpyrimidin-2-onyl, phenyl, fluorophenyl, hydroxymethyl, tetrahydropyranyloxymethyl, imidazolylmethyl,

pyrrolylmethyl, -CH=N-OCH<sub>3</sub> and  ;

W is chosen from H, Cl, F, R<sup>8</sup>, C<sub>1</sub>-C<sub>4</sub>-alkylaryl, -OR<sup>8</sup>, -SR<sup>8</sup>, -NR<sup>9</sup>R<sup>10</sup> and -NHC(O)R<sup>11</sup>, with the proviso that when Q is imidazolyl, W is not H, Cl, F or R<sup>8</sup>;

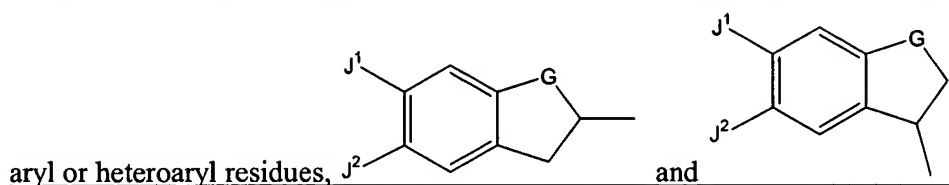
R<sup>1</sup> is chosen from alkyl, cycloalkyl, alkenyl, C<sub>1</sub>-C<sub>3</sub>-alkylcycloalkyl, heterocyclyl, C<sub>1</sub>-C<sub>3</sub>-alkylheterocyclyl, aryl, C<sub>1</sub>-C<sub>3</sub>-alkylaryl, heteroaryl, C<sub>1</sub>-C<sub>3</sub>-alkylheteroaryl,

(C<sub>1</sub>-C<sub>3</sub>-alkyloxy)alkyl, (C<sub>1</sub>-C<sub>3</sub>-alkyloxy)cycloalkyl, (C<sub>1</sub>-C<sub>3</sub>-alkylthio)alkyl, (C<sub>1</sub>-C<sub>3</sub>-alkylthio)cycloalkyl and (C<sub>1</sub>-C<sub>3</sub>-alkylsulfonyl)alkyl;

R<sup>2</sup> is H or C<sub>1</sub>-C<sub>3</sub>-alkyl, or R<sup>1</sup> and R<sup>2</sup> taken together form a 5- to 7-membered ring structure optionally containing O, S or NR<sup>12</sup>;

R<sup>3</sup> is H or C<sub>1</sub>-C<sub>6</sub>-alkyl, or, when n is zero, R<sup>2</sup> and R<sup>3</sup> taken together may form a 6-membered ring, which may be fused to a six-membered saturated or aromatic carbocycle;

R<sup>4</sup> is chosen from H, aryl, heteroaryl, C<sub>1</sub>-C<sub>4</sub>-alkyl substituted with from one to three



, wherein J<sup>1</sup> and J<sup>2</sup> are independently chosen from H, F, Cl, CN, NO<sub>2</sub> and CH<sub>3</sub>, and G is chosen from -CH<sub>2</sub>-, -CH<sub>2</sub>CH<sub>2</sub>-, -CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>-, -OCH<sub>2</sub>-, -CH<sub>2</sub>O-, -CH<sub>2</sub>CH<sub>2</sub>O-, -OCH<sub>2</sub>CH<sub>2</sub>-, -O-, -N(lower alkyl)-, -N(lower alkyl)CH<sub>2</sub>-, -CH<sub>2</sub>N(lower alkyl)-, -S-, -SO-, -SO<sub>2</sub>-, -CH<sub>2</sub>S-, -SCH<sub>2</sub>-, -CH<sub>2</sub>SO-, -SOCH<sub>2</sub>-, -CH<sub>2</sub>SO<sub>2</sub>-, and -SO<sub>2</sub>CH<sub>2</sub>-;

R<sup>5</sup> is H or C<sub>1</sub>-C<sub>3</sub>-alkyl, with the proviso that both R<sup>3</sup> and R<sup>5</sup> cannot be alkyl;

R<sup>6</sup> is aryl;

R<sup>7</sup> is aryl or C<sub>1</sub>-C<sub>3</sub>-alkylaryl;

R<sup>8</sup> is chosen from alkyl, aryl, heteroaryl, substituted alkyl, C<sub>1</sub>-C<sub>4</sub>-alkylaryl, C<sub>1</sub>-C<sub>4</sub>-alkylheterocyclyl and C<sub>1</sub>-C<sub>4</sub>-alkylheteroaryl;

R<sup>9</sup> is chosen from H, alkyl, alkenyl, substituted alkyl, cycloalkyl, aryl, alkoxy, heteroaryl, fluoroalkyl, C<sub>1</sub>-C<sub>4</sub>-alkylcycloalkyl, (C<sub>1</sub>-C<sub>4</sub>-alkoxy)alkyl, (C<sub>1</sub>-C<sub>4</sub>-alkoxycarbonyl)alkyl, (C<sub>1</sub>-C<sub>4</sub>-alkylthio)alkyl, heterocyclyl, C<sub>1</sub>-C<sub>4</sub>-alkylheterocyclyl, C<sub>1</sub>-C<sub>4</sub>-alkylaryl, and C<sub>1</sub>-C<sub>4</sub>-alkylheteroaryl;

R<sup>10</sup> is H or C<sub>1</sub>-C<sub>3</sub>-alkyl, or

R<sup>9</sup> and R<sup>10</sup> taken together may form a 5- to 7-membered ring structure optionally containing O, S, SO, SO<sub>2</sub> or NR<sup>12</sup>, said ring optionally substituted with -OH, -CN, -COOH or -COOCH<sub>3</sub>;

$R^{11}$  is aryl;

$R^{12}$  is chosen from H,  $C_1$ - $C_3$ -alkyl, alkoxycarbonyl, methoxyacetyl and aryl;

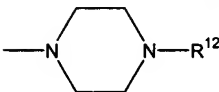
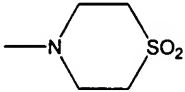
m is zero or one; and

n is zero or one, with the proviso that when A is  $A^2$ , m and n cannot both be zero.

5. (original) A 4-pyrimidinamine according to claim 4 wherein:

Q is chosen from pyrrol-1-yl, imidazol-1-yl, furan-3-yl, 2-methylimidazol-1-yl and 4-methylimidazol-1-yl;

A is  $R^4R^5N-C(O)-$ ;

W is Cl,  $NHR^9$ ,  $N(CH_3)R^9$ ,  $OR^8$ ,  $SR^8$ ,  $R^8$ , morpholin-4-yl,  ;  or

$R^1$  is chosen from alkyl, cycloalkyl,  $C_1$ - $C_3$ -alkylaryl,  $C_1$ - $C_3$ -alkylcycloalkyl,  $C_1$ - $C_3$ -alkylheterocyclyl,  $C_1$ - $C_3$ -alkylheteroaryl ;

$R^2$ ,  $R^3$  and  $R^5$  are H;

$R^8$  is  $C_1$ - $C_4$ -alkylaryl

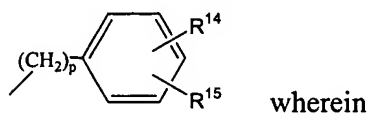
$R^9$  is chosen from hydrogen, alkyl, substituted alkyl,  $(C_1-C_4)$ -alkoxy,  $C_1$ - $C_4$ -alkylcycloalkyl,  $C_1$ - $C_4$ -alkylaryl, heterocyclyl,  $C_1$ - $C_4$ -alkylheteroaryl,  $C_1$ - $C_4$ -alkylheterocyclyl; and

m and n are zero.

6. (original) A 4-pyrimidinamine according to claim 5 wherein W is  $NHR^9$  and

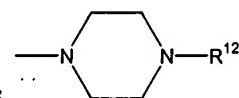
$R^9$  is chosen from hydrogen; methyl; ethyl; 2,2,2-trifluoroethyl; allyl; cyclopropyl; 2-cyanoethyl; propargyl; methoxy; methoxyethyl; cyclopropyl; cyclopropylmethyl; (methylthio)ethyl; 3-methoxypropyl; 3-pyridyl; 2-(3-pyridyl)ethyl; 2-(2-pyridyl)ethyl; 3-pyridylmethyl; 4-pyridylmethyl; 4-pyridylmethyl-N-oxide; 2-pyridazinylmethyl; sulfolan-3-yl; 3-tetrahydrofuranyl; 2-tetrahydrofuranylmethyl; 3-(1-imidazolyl)propyl; 1-*t*-

butoxycarbonyl-4-piperidinyl; 1-*t*-butoxycarbonyl-4-piperidinylmethyl; 2-(hydroxyimino)propyl; 2-(methoxyimino)propyl; 2-oxo-1-propyl; and

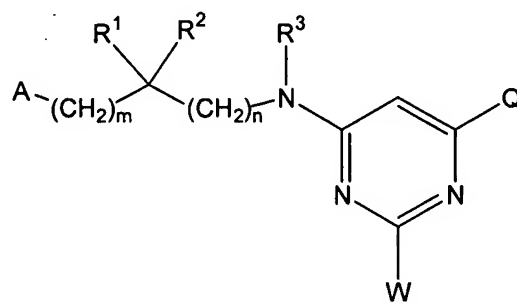


- $R^{14}$  is chosen from H, Cl, F, CN, NO<sub>2</sub>, SO<sub>2</sub>NH<sub>2</sub>, CF<sub>3</sub>, COOCH<sub>3</sub>, OCH<sub>3</sub>, OH, SO<sub>2</sub>CH<sub>3</sub>, N(CH<sub>3</sub>)<sub>2</sub> and COOH;  
 $R^{15}$  is chosen from H, OCH<sub>3</sub> and Cl; and  
 $p$  is 1 or 2.

7. (original) A 4-pyrimidinamine according to claim 5 wherein W is and  
 $R^{12}$  is *t*-butoxycarbonyl, methoxyacetyl or phenyl.



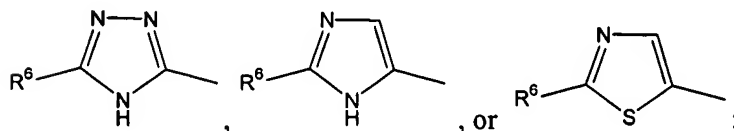
8. (currently amended) ~~A 4-pyrimidinamine according to claim 1 wherein~~ A compound of formula



wherein:

Z is CH<sub>2</sub>;

A is



- $R^1$  is chosen from *n*-butyl; cyclohexylmethyl; cyclopentylmethyl; 2-methylpropyl; 3-methyl-1-butyl; cyclohexyl; 2,2-dimethylpropyl; benzyl; 2-thienylmethyl; 1-

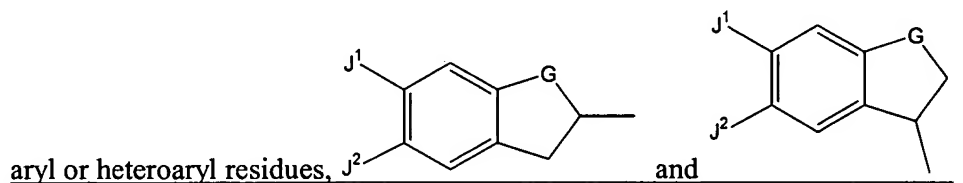
*t*-butoxycarbonyl-4-piperidinyl; 4-chlorobenzyl; 2-pyranylmethyl; 4-pyranylmethyl; 4-pyranyl and 1,1-dimethylethyl;

R<sup>2</sup> and R<sup>3</sup> are H;

Q is imidazolyl or pyrrolyl;

R<sup>6</sup> is aryl;

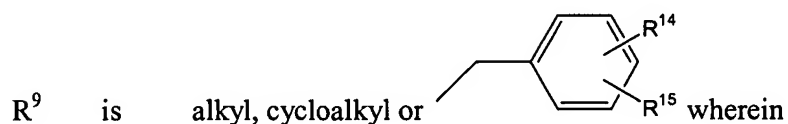
R<sup>4</sup> is chosen from H, aryl, heteroaryl, C<sub>1</sub>-C<sub>4</sub>-alkyl substituted with from one to three



, wherein J<sup>1</sup> and J<sup>2</sup> are independently chosen from H, F, Cl, CN, NO<sub>2</sub> and CH<sub>3</sub>, and G is chosen from -CH<sub>2</sub>-, -CH<sub>2</sub>CH<sub>2</sub>-, -CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>-, -OCH<sub>2</sub>-, -CH<sub>2</sub>O-, -CH<sub>2</sub>CH<sub>2</sub>O-, -OCH<sub>2</sub>CH<sub>2</sub>-, -O-, -N(lower alkyl)-, -N(lower alkyl)CH<sub>2</sub>-, -CH<sub>2</sub>N(lower alkyl)-, -S-, -SO-, -SO<sub>2</sub>-, -CH<sub>2</sub>S-, -SCH<sub>2</sub>-, -CH<sub>2</sub>SO-, -SOCH<sub>2</sub>-, -CH<sub>2</sub>SO<sub>2</sub>-, and -SO<sub>2</sub>CH<sub>2</sub>-;

R<sup>7</sup> is aryl or C<sub>1</sub>-C<sub>3</sub>-alkylaryl;

W is NHR<sup>9</sup>; and



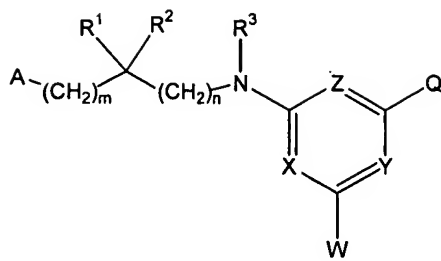
R<sup>14</sup> is chosen from H, Cl, F, CN, NO<sub>2</sub>, SO<sub>2</sub>NH<sub>2</sub>, CF<sub>3</sub>, COOCH<sub>3</sub>, OCH<sub>3</sub>, SO<sub>2</sub>CH<sub>3</sub>, N(CH<sub>3</sub>)<sub>2</sub> and COOH; and

R<sup>15</sup> is chosen from H, OCH<sub>3</sub> and Cl.

m is zero or one; and

n is zero or one, with the proviso that when A is chosen from R<sup>7</sup>C(O)NH-, R<sup>7</sup>S(O)<sub>2</sub>NH-, R<sup>4</sup>NH-, and R<sup>4</sup>O-, m and n cannot both be zero.

9. (currently amended) ~~A pyrimidine according to claim 1 wherein:~~ A compound of formula

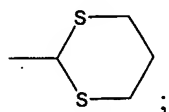


wherein:

two of X, Y and Z are N and the other of X, Y and Z is CH;

A is  $R^4R^5N-C(O)-$ ;

Q is chosen from heteroaryl, aryl,  $-CH_2R^{13}$ ,  $-CH=N-OCH_3$  and

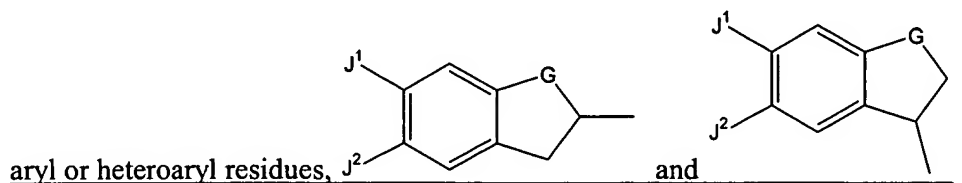


W is chosen from H, Cl, F,  $R^8$ ,  $C_1-C_4$ -alkylaryl,  $-OR^8$ ,  $-SR^8$ ,  $-NR^9R^{10}$  and  $-NHC(O)R^{11}$ , with the proviso that when Q is imidazolyl, W is not H, Cl, F or  $R^8$ ;

$R^1$  is chosen from isopropyl; n-butyl; cyclohexylmethyl; cyclopentylmethyl; naphthylmethyl; cyclohexylethyl; 2-methylpropyl; 3-methyl-1-butyl; cyclohexyl; 2,2-dimethylpropyl; benzyl; 2-thienylmethyl; 1-*t*-butoxycarbonyl-4-piperidinyl; 4-methoxybenzyl; 4-chlorobenzyl; 3,4-dichlorobenzyl; 2-pyranylmethyl; 4-pyranylmethyl; 4-pyranyl and 1,1-dimethylethyl; and

$R^2$ ,  $R^3$  and  $R^5$  are H;

$R^4$  is chosen from H, aryl, heteroaryl,  $C_1-C_4$ -alkyl substituted with from one to three



aryl or heteroaryl residues, and

, wherein  $J^1$  and  $J^2$  are independently chosen from H, F, Cl, CN,  $NO_2$  and  $CH_3$ , and G is chosen from  $-CH_2-$ ,  $-CH_2CH_2-$ ,  $-CH_2CH_2CH_2-$ ,  $-OCH_2-$ ,  $-CH_2O-$ ,  $-CH_2CH_2O-$ ,  $-OCH_2CH_2-$ ,  $-O-$ ,  $-N(lower\ alkyl)-$ ,  $-N(lower\ alkyl)CH_2-$ ,  $-CH_2N(lower\ alkyl)-$ ,  $-S-$ ,  $-SO-$ ,  $-SO_2-$ ,  $-CH_2S-$ ,  $-SCH_2-$ ,  $-CH_2SO-$ ,  $-SOCH_2-$ ,  $-CH_2SO_2-$ , and  $-SO_2CH_2-$ ;

$R^7$  is aryl or  $C_1-C_3$ -alkylaryl;

$R^8$  is chosen from alkyl, aryl, heteroaryl, substituted alkyl,  $C_1$ - $C_4$ -alkylaryl,  $C_1$ - $C_4$ -alkylheterocyclyl and  $C_1$ - $C_4$ -alkylheteroaryl;

$R^9$  is chosen from H, alkyl, alkenyl, substituted alkyl, cycloalkyl, aryl, alkoxy, heteroaryl, fluoroalkyl,  $C_1$ - $C_4$ -alkylcycloalkyl,  $(C_1$ - $C_4$ -alkoxy)alkyl,  $(C_1$ - $C_4$ -alkoxycarbonyl)alkyl,  $(C_1$ - $C_4$ -alkylthio)alkyl, heterocyclyl,  $C_1$ - $C_4$ -alkylheterocyclyl,  $C_1$ - $C_4$ -alkylaryl, and  $C_1$ - $C_4$ -alkylheteroaryl;

$R^{10}$  is H or  $C_1$ - $C_3$ -alkyl, or

$R^9$  and  $R^{10}$  taken together may form a 5- to 7-membered ring structure optionally containing O, S, SO,  $SO_2$  or  $NR^{12}$ , said ring optionally substituted with -OH, -CN, -COOH or -COOCH<sub>3</sub>;

$R^{11}$  is aryl;

$R^{12}$  is chosen from H,  $C_1$ - $C_3$ -alkyl, alkoxycarbonyl, methoxyacetyl and aryl;

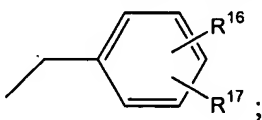
$R^{13}$  is chosen from -OH, -OTHP, 1-imidazolyl, and 1-pyrrolyl;

m is zero or one; and

n is zero or one, with the proviso that when A is chosen from  $R^7C(O)NH$ -,  $R^7S(O)_2NH$ -,  $R^4NH$ -, and  $R^4O$ -, m and n cannot both be zero.

10. (original) A pyrimidine according to claim 9 wherein:

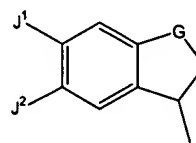
$R^4$  is pyridinyl, pyridinylmethyl, tetrahydronaphthalenyl, indanylmethyl,

furanylmethyl, substituted phenyl, or  ;

$R^{16}$  is chosen from H, Cl, F, CN, NO<sub>2</sub>, SO<sub>2</sub>NH<sub>2</sub>, CF<sub>3</sub>, CH<sub>3</sub>, COOCH<sub>3</sub>, OCH<sub>3</sub>, SO<sub>2</sub>CH<sub>3</sub>, SOCH<sub>3</sub>, N(CH<sub>3</sub>)<sub>2</sub>, tetrazol-5-yl, CONH<sub>2</sub>, C(=NOH)NH<sub>2</sub> and COOH; and

$R^{17}$  is chosen from H, OCH<sub>3</sub>, F and Cl.

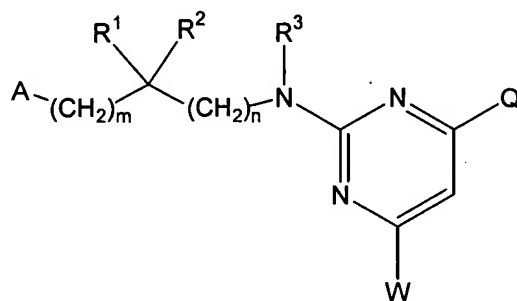
11. (original) A pyrimidine according to claim 9 wherein  $R^4$  is



, one of

$J^1$  and  $J^2$  is H and the other is H, Cl or CN and G is chosen from  $-\text{CH}_2-$ ,  $-\text{CH}_2\text{CH}_2-$ ,  $-\text{OCH}_2-$ ,  $-\text{O}-$  and  $-\text{CH}_2\text{N}(\text{lower alkyl})-$ .

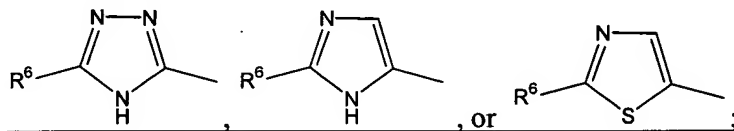
12. (currently amended) ~~A 2-pyrimidinamine according to claim 1, wherein Y is CH,~~  
 having the formula A compound of formula



wherein:

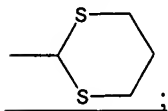
A is  $A^1$  or  $A^2$ ;

$A^1$  is  $\text{R}^4\text{R}^5\text{N}-\text{C}(\text{O})-$ ,



$A^2$  is chosen from  $\text{R}^7\text{C}(\text{O})\text{NH}-$ ,  $\text{R}^7\text{S}(\text{O})_2\text{NH}-$ ,  $\text{R}^4\text{NH}-$ , and  $\text{R}^4\text{O}-$ ;

Q is chosen from heteroaryl, aryl,  $-\text{CH}_2\text{R}^{13}$ ,  $-\text{CH}=\text{N}-\text{OCH}_3$  and



W is chosen from H, Cl, F,  $\text{R}^8$ ,  $\text{C}_1\text{-C}_4\text{-alkylaryl}$ ,  $-\text{OR}^8$ ,  $-\text{SR}^8$ ,  $-\text{NR}^9\text{R}^{10}$  and  $-\text{NHC}(\text{O})\text{R}^{11}$ , with the proviso that when Q is imidazolyl, W is not H, Cl, F or  $\text{R}^8$ ;

$\text{R}^1$  is chosen from alkyl, cycloalkyl, alkenyl,  $\text{C}_1\text{-C}_3\text{-alkylcycloalkyl}$ , heterocyclyl,  $\text{C}_1\text{-C}_3\text{-alkylheterocyclyl}$ , aryl,  $\text{C}_1\text{-C}_3\text{-alkylaryl}$ , heteroaryl,  $\text{C}_1\text{-C}_3\text{-alkylheteroaryl}$ ,  $(\text{C}_1\text{-C}_3\text{-alkyloxy})\text{alkyl}$ ,  $(\text{C}_1\text{-C}_3\text{-alkyloxy})\text{cycloalkyl}$ ,  $(\text{C}_1\text{-C}_3\text{-alkylthio})\text{alkyl}$ ,  $(\text{C}_1\text{-C}_3\text{-alkylthio})\text{cycloalkyl}$  and  $(\text{C}_1\text{-C}_3\text{-alkylsulfonyl})\text{alkyl}$ ;

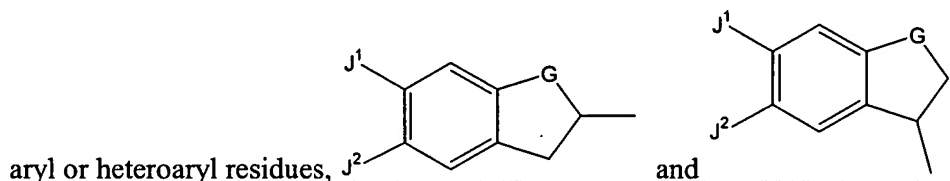
$\text{R}^2$  is H or  $\text{C}_1\text{-C}_3\text{-alkyl}$ , or  $\text{R}^1$  and  $\text{R}^2$  taken together form a 5- to 7-membered ring



structure optionally containing O, S or NR<sup>12</sup>.

R<sup>3</sup> is H or C<sub>1</sub>-C<sub>6</sub>-alkyl, or, when n is zero, R<sup>2</sup> and R<sup>3</sup> taken together may form a 6-membered ring, which may be fused to a six-membered saturated or aromatic carbocycle;

R<sup>4</sup> is chosen from H, aryl, heteroaryl, C<sub>1</sub>-C<sub>4</sub>-alkyl substituted with from one to three



, wherein J<sup>1</sup> and J<sup>2</sup> are independently chosen from H, F, Cl, CN, NO<sub>2</sub> and CH<sub>3</sub>, and G is chosen from -CH<sub>2</sub>-, -CH<sub>2</sub>CH<sub>2</sub>-, -CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>-, -OCH<sub>2</sub>-, -CH<sub>2</sub>O-, -CH<sub>2</sub>CH<sub>2</sub>O-, -OCH<sub>2</sub>CH<sub>2</sub>-, -O-, -N(lower alkyl)-, -N(lower alkyl)CH<sub>2</sub>-, -CH<sub>2</sub>N(lower alkyl)-, -S-, -SO-, -SO<sub>2</sub>-, -CH<sub>2</sub>S-, -SCH<sub>2</sub>-, -CH<sub>2</sub>SO-, -SOCH<sub>2</sub>-, -CH<sub>2</sub>SO<sub>2</sub>-, and -SO<sub>2</sub>CH<sub>2</sub>-;

R<sup>5</sup> is H or C<sub>1</sub>-C<sub>3</sub>-alkyl, with the proviso that both R<sup>3</sup> and R<sup>5</sup> cannot be alkyl;

R<sup>6</sup> is aryl;

R<sup>7</sup> is aryl or C<sub>1</sub>-C<sub>3</sub>-alkylaryl;

R<sup>8</sup> is chosen from alkyl, aryl, heteroaryl, substituted alkyl, C<sub>1</sub>-C<sub>4</sub>-alkylaryl, C<sub>1</sub>-C<sub>4</sub>-alkylheterocyclyl and C<sub>1</sub>-C<sub>4</sub>-alkylheteroaryl;

R<sup>9</sup> is chosen from H, alkyl, alkenyl, substituted alkyl, cycloalkyl, aryl, alkoxy, heteroaryl, fluoroalkyl, C<sub>1</sub>-C<sub>4</sub>-alkylcycloalkyl, (C<sub>1</sub>-C<sub>4</sub>-alkoxy)alkyl, (C<sub>1</sub>-C<sub>4</sub>-alkoxycarbonyl)alkyl, (C<sub>1</sub>-C<sub>4</sub>-alkylthio)alkyl, heterocyclyl, C<sub>1</sub>-C<sub>4</sub>-alkylheterocyclyl, C<sub>1</sub>-C<sub>4</sub>-alkylaryl, and C<sub>1</sub>-C<sub>4</sub>-alkylheteroaryl;

R<sup>10</sup> is H or C<sub>1</sub>-C<sub>3</sub>-alkyl, or

R<sup>9</sup> and R<sup>10</sup> taken together may form a 5- to 7-membered ring structure optionally containing O, S, SO, SO<sub>2</sub> or NR<sup>12</sup>, said ring optionally substituted with -OH, -CN, -COOH or -COOCH<sub>3</sub>;

R<sup>11</sup> is aryl;

R<sup>12</sup> is chosen from H, C<sub>1</sub>-C<sub>3</sub>-alkyl, alkoxycarbonyl, methoxyacetyl and aryl;

R<sup>13</sup> is chosen from -OH, -OTHP, 1-imidazolyl, and 1-pyrrolyl;

m is zero or one; and

n is zero or one, with the proviso that when A is A<sup>2</sup>, m and n cannot both be zero.

13. (previously amended) A 2-pyrimidinamine according to claim 12 wherein Q is chosen from imidazolyl, pyrrolyl, pyridinyl, fluorophenyl and 2-thienyl.

14. (original) A 2-pyrimidinamine according to claim 13 wherein

A is R<sup>4</sup>R<sup>5</sup>N-C(O)-;

W is H, Cl, NHR<sup>9</sup> or OR<sup>8</sup>;

R<sup>1</sup> is chosen from alkyl and C<sub>1</sub>-C<sub>3</sub>-alkylcycloalkyl;

R<sup>2</sup>, R<sup>3</sup> and R<sup>5</sup> are H;

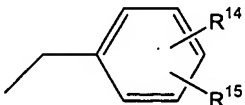
R<sup>4</sup> is C<sub>1</sub>-C<sub>4</sub>-alkylaryl or C<sub>1</sub>-C<sub>4</sub>-alkylheteroaryl;

R<sup>8</sup> is C<sub>1</sub>-C<sub>4</sub>-alkylaryl;

R<sup>9</sup> is chosen from hydrogen, alkyl, fluoroalkyl, (C<sub>1</sub>-C<sub>4</sub>-alkoxy)alkyl, (C<sub>1</sub>-C<sub>4</sub>-alkylthio)alkyl, C<sub>1</sub>-C<sub>4</sub>-alkylcycloalkyl, C<sub>1</sub>-C<sub>4</sub>-alkylaryl, heterocyclyl, C<sub>1</sub>-C<sub>4</sub>-alkylheteroaryl, C<sub>1</sub>-C<sub>4</sub>-alkylheterocyclyl; and

m and n are zero.

15. (original) A 2-pyrimidinamine according to claim 14 wherein W is NHR<sup>9</sup> and

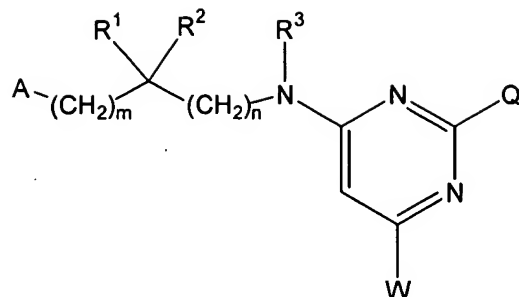
R<sup>9</sup> is  wherein

R<sup>14</sup> is chosen from H, F, Cl, CN, NO<sub>2</sub>, SO<sub>2</sub>NH<sub>2</sub>, CF<sub>3</sub>, COOCH<sub>3</sub>, OCH<sub>3</sub>, SO<sub>2</sub>CH<sub>3</sub>, N(CH<sub>3</sub>)<sub>2</sub> and COOH; and

R<sup>15</sup> is chosen from H, OCH<sub>3</sub> and Cl.

16-17. (canceled)

18. (currently amended) ~~A 4-pyrimidinamine according to claim 17 wherein: A~~  
compound of formula



wherein:

A is  $R^4R^5N-C(O)-$ ;

Q is chosen from imidazolyl and pyrrolyl;

W is  $NHR^9$ ;

$R^1$  is chosen from cyclohexylmethyl; 2-methylpropyl and 3-methyl-1-butyl;

$R^2$ ,  $R^3$  and  $R^5$  are H; and

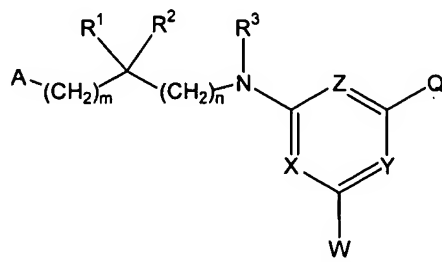
$R^4$  and  $R^9$  are benzyl or substituted benzyl;

m is zero; and

n is zero.

19-25. (canceled)

26. (currently amended) ~~A compound according to claim 1 wherein~~ A compound of formula

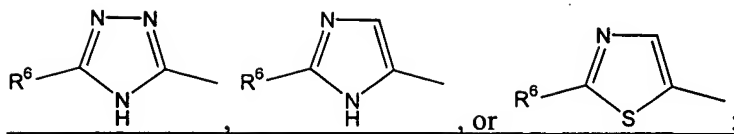


wherein:

two of X, Y and Z are N and the other of X, Y and Z is CH;

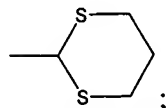
A is  $A^1$  or  $A^2$ ;

$A^1$  is  $R^4R^5N-C(O)-$ .



$A^2$  is chosen from  $R^7C(O)NH-$ ,  $R^7S(O)_2NH-$ ,  $R^4NH-$ , and  $R^4O-$ ;

$Q$  is chosen from heteroaryl, aryl,  $-CH_2R^{13}$ ,  $-CH=N-OCH_3$  and

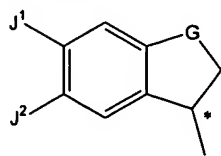


$W$  is chosen from H, Cl, F,  $R^8$ ,  $C_1-C_4$ -alkylaryl,  $-OR^8$ ,  $-SR^8$ ,  $-NR^9R^{10}$  and  $-NHC(O)R^{11}$ , with the proviso that when  $Q$  is imidazolyl,  $W$  is not H, Cl, F or  $R^8$ ;

$R^1$  is chosen from alkyl, cycloalkyl, alkenyl,  $C_1-C_3$ -alkylcycloalkyl, heterocyclyl,  $C_1-C_3$ -alkylheterocyclyl, aryl,  $C_1-C_3$ -alkylaryl, heteroaryl,  $C_1-C_3$ -alkylheteroaryl,  $(C_1-C_3$ -alkyloxy)alkyl,  $(C_1-C_3$ -alkyloxy)cycloalkyl,  $(C_1-C_3$ -alkylthio)alkyl,  $(C_1-C_3$ -alkylthio)cycloalkyl and  $(C_1-C_3$ -alkylsulfonyl)alkyl;

$R^2$  is H or  $C_1-C_3$ -alkyl, or  $R^1$  and  $R^2$  taken together form a 5- to 7-membered ring structure optionally containing O, S or  $NR^{12}$ ;

$R^3$  is H or  $C_1-C_6$ -alkyl, or, when  $n$  is zero,  $R^2$  and  $R^3$  taken together may form a 6-membered ring, which may be fused to a six-membered saturated or aromatic carbocycle;



$R^4$  is is having the R configuration at the carbon indicated with an asterisk, wherein  $J^1$  and  $J^2$  are independently chosen from H, F, Cl, CN,  $NO_2$  and  $CH_3$ , and  $G$  is chosen from  $-CH_2-$ ,  $-CH_2CH_2-$ ,  $-CH_2CH_2CH_2-$ ,  $-OCH_2-$ ,  $-CH_2O-$ ,  $-CH_2CH_2O-$ ,  $-OCH_2CH_2-$ ,  $-O-$ ,  $-N$ (lower alkyl)-,  $-N$ (lower alkyl) $CH_2-$ ,  $-CH_2N$ (lower alkyl)-,  $-S-$ ,  $-SO-$ ,  $-SO_2-$ ,  $-CH_2S-$ ,  $-SCH_2-$ ,  $-CH_2SO-$ ,  $-SOCH_2-$ ,  $-CH_2SO_2-$ , and  $-SO_2CH_2-$ ;

$R^5$  is H or  $C_1-C_3$ -alkyl, with the proviso that both  $R^3$  and  $R^5$  cannot be alkyl;

$R^6$  is aryl;

$R^7$  is aryl or  $C_1-C_3$ -alkylaryl;

$R^8$  is chosen from alkyl, aryl, heteroaryl, substituted alkyl,  $C_1$ - $C_4$ -alkylaryl,  $C_1$ - $C_4$ -alkylheterocyclyl and  $C_1$ - $C_4$ -alkylheteroaryl;

$R^9$  is chosen from H, alkyl, alkenyl, substituted alkyl, cycloalkyl, aryl, alkoxy, heteroaryl, fluoroalkyl,  $C_1$ - $C_4$ -alkylcycloalkyl,  $(C_1$ - $C_4$ -alkoxy)alkyl,  $(C_1$ - $C_4$ -alkoxycarbonyl)alkyl,  $(C_1$ - $C_4$ -alkylthio)alkyl, heterocyclyl,  $C_1$ - $C_4$ -alkylheterocyclyl,  $C_1$ - $C_4$ -alkylaryl, and  $C_1$ - $C_4$ -alkylheteroaryl;

$R^{10}$  is H or  $C_1$ - $C_3$ -alkyl, or

$R^9$  and  $R^{10}$  taken together may form a 5- to 7-membered ring structure optionally containing O, S, SO, SO<sub>2</sub> or NR<sup>12</sup>, said ring optionally substituted with -OH, -CN, -COOH or -COOCH<sub>3</sub>;

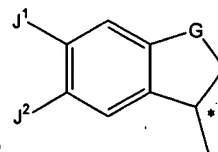
$R^{11}$  is aryl;

$R^{12}$  is chosen from H,  $C_1$ - $C_3$ -alkyl, alkoxycarbonyl, methoxyacetyl and aryl;

$R^{13}$  is chosen from -OH, -OTHP, 1-imidazolyl, and 1-pyrrolyl;

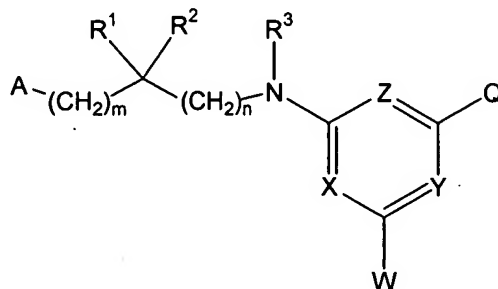
m is zero or one; and

n is zero or one, with the proviso that when A is A<sup>2</sup>, m and n cannot both be zero.



27. (original) A pyrimidine according to claim 12 wherein  $R^4$  is the R configuration at the carbon indicated with an asterisk.

28. (currently amended) A compound of formula

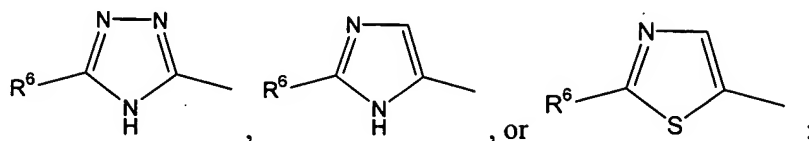


wherein:

two of X, Y and Z are N and the other of X, Y and Z is CH;

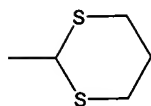
A is  $A^1$  or  $A^2$ ;

$A^1$  is  $R^4R^5N-C(O)-$ ,



$A^2$  is chosen from  $R^7C(O)NH-$ ,  $R^7S(O)_2NH-$ ,  $R^4NH-$ , and  $R^4O-$ ;

Q is chosen from aryl,  $-CH_2R^{13}$ ,  $-CH=N-OCH_3$  and



heteroaryl other than 1-imidazolyl and 1-triazolyl;

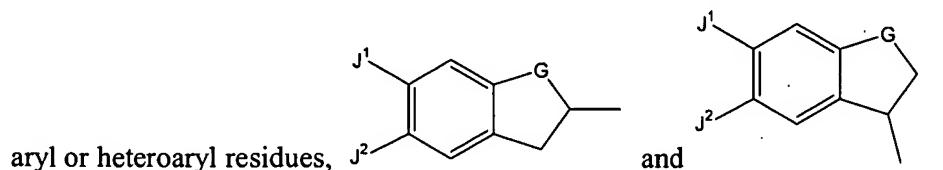
W is chosen from H, Cl, F,  $R^8$ ,  $C_1-C_4$ -alkylaryl,  $-OR^8$ ,  $-SR^8$ ,  $-NR^9R^{10}$  and  $-NHC(O)R^{11}$ , with the proviso that when Q is imidazolyl, W ~~may not be~~ is not H, Cl, F or  $R^8$ ;

$R^1$  is chosen from alkyl, cycloalkyl, alkenyl,  $C_1-C_3$ -alkylcycloalkyl, heterocyclyl,  $C_1-C_3$ -alkylheterocyclyl, aryl,  $C_1-C_3$ -alkylaryl, heteroaryl,  $C_1-C_3$ -alkylheteroaryl,  $(C_1-C_3$ -alkyloxy)alkyl,  $(C_1-C_3$ -alkyloxy)cycloalkyl,  $(C_1-C_3$ -alkylthio)alkyl,  $(C_1-C_3$ -alkylthio)cycloalkyl and  $(C_1-C_3$ -alkylsulfonyl)alkyl;

$R^2$  is H or  $C_1-C_3$ -alkyl, or  $R^1$  and  $R^2$  taken together form a 5- to 7-membered ring structure optionally containing O, S or  $NR^{12}$ ;

$R^3$  is H or  $C_1-C_6$ -alkyl, or, when n is zero,  $R^2$  and  $R^3$  taken together may form a 6-membered ring, which may be fused to a six-membered saturated or aromatic carbocycle;

$R^4$  is chosen from H, aryl, heteroaryl,  $C_1-C_4$ -alkyl substituted with from one to three



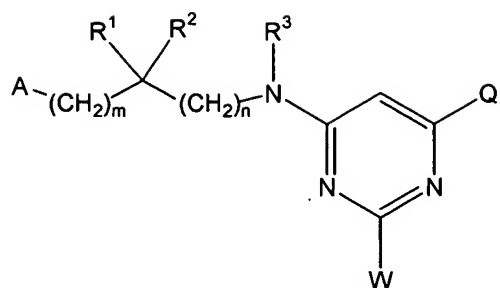
wherein  $J^1$  and  $J^2$  are independently chosen from H, F, Cl, CN,  $NO_2$  and  $CH_3$ , and G is chosen from  $-CH_2-$ ,  $-CH_2CH_2-$ ,  $-CH_2CH_2CH_2-$ ,  $-OCH_2-$ ,  $-CH_2O-$ ,  $-CH_2CH_2O-$ ,  $-OCH_2CH_2-$ ,  $-O-$ ,  $-N$ (lower alkyl)-,  $-N$ (lower alkyl) $CH_2-$ , -

CH<sub>2</sub>N(lower alkyl)-, -S-, -SO-, -SO<sub>2</sub>-, -CH<sub>2</sub>S-, -SCH<sub>2</sub>-, -CH<sub>2</sub>SO-, -SOCH<sub>2</sub>-, -CH<sub>2</sub>SO<sub>2</sub>-, and -SO<sub>2</sub>CH<sub>2</sub>-;

- R<sup>5</sup> is H or C<sub>1</sub>-C<sub>3</sub>-alkyl, with the proviso that both R<sup>3</sup> and R<sup>5</sup> cannot be alkyl;
- R<sup>6</sup> is aryl;
- R<sup>7</sup> is aryl or C<sub>1</sub>-C<sub>3</sub>-alkylaryl;
- R<sup>8</sup> is chosen from alkyl, aryl, heteroaryl, substituted alkyl, C<sub>1</sub>-C<sub>4</sub>-alkylaryl, C<sub>1</sub>-C<sub>4</sub>-alkylheterocyclyl and C<sub>1</sub>-C<sub>4</sub>-alkylheteroaryl;
- R<sup>9</sup> is chosen from H, alkyl, alkenyl, substituted alkyl, cycloalkyl, aryl, alkoxy, heteroaryl, fluoroalkyl, C<sub>1</sub>-C<sub>4</sub>-alkylcycloalkyl, (C<sub>1</sub>-C<sub>4</sub>-alkoxy)alkyl, (C<sub>1</sub>-C<sub>4</sub>-alkoxycarbonyl)alkyl, (C<sub>1</sub>-C<sub>4</sub>-alkylthio)alkyl, heterocyclyl, C<sub>1</sub>-C<sub>4</sub>-alkylheterocyclyl, C<sub>1</sub>-C<sub>4</sub>-alkylaryl, and C<sub>1</sub>-C<sub>4</sub>-alkylheteroaryl;
- R<sup>10</sup> is H or C<sub>1</sub>-C<sub>3</sub>-alkyl, or
- R<sup>9</sup> and R<sup>10</sup> taken together may form a 5- to 7-membered ring structure optionally containing O, S, SO, SO<sub>2</sub> or NR<sup>12</sup>, said ring optionally substituted with -OH, -CN, -COOH or -COOCH<sub>3</sub>;
- R<sup>11</sup> is aryl;
- R<sup>12</sup> is chosen from H, C<sub>1</sub>-C<sub>3</sub>-alkyl, alkoxycarbonyl, methoxyacetyl and aryl;
- R<sup>13</sup> is chosen from -OH, -OTHP, 1-imidazolyl, and 1-pyrrolyl;
- m is zero or one; and
- n is zero or one, with the proviso that when A is A<sup>2</sup>, m and n cannot both be zero.

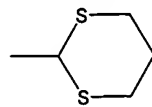
29. (canceled)

30. (previously amended) A 4-pyrimidinamine according to claim 28, wherein Z is CH, having the formula



31. (original) A 4-pyrimidinamine according to claim 30 wherein Q is chosen from methylimidazolyl, pyrrolyl, methylpyrrolyl, pyrazolyl, methylpyrazolyl, furanyl, methylfuranyl, thienyl, oxazolyl, thiazolyl, pyridinyl, quinolinyl, 1-methylpyrimidin-2-onyl, phenyl, fluorophenyl, hydroxymethyl, 2-imidazolyl, tetrahydropyranyloxymethyl,

imidazolylmethyl, pyrrolylmethyl,  $-\text{CH}=\text{N}-\text{OCH}_3$  and

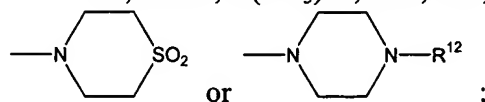


32. (original) A 4-pyrimidinamine according to claim 31 wherein:

Q is chosen from pyrrol-1-yl, imidazol-1-yl, furan-3-yl, 2-methylimidazol-1-yl and 4-methylimidazol-1-yl;

A is  $\text{R}^4\text{R}^5\text{N}-\text{C}(\text{O})-$ ;

W is  $\text{Cl}$ ,  $\text{NHR}^9$ ,  $\text{N}(\text{CH}_3)\text{R}^9$ ,  $\text{OR}^8$ ,  $\text{SR}^8$ ,  $\text{R}^8$ , morpholin-4-yl,



$\text{R}^1$  is chosen from alkyl, cycloalkyl,  $\text{C}_1\text{-C}_3$ -alkylaryl,  $\text{C}_1\text{-C}_3$ -alkylcycloalkyl,  $\text{C}_1\text{-C}_3$ -alkylheterocyclyl,  $\text{C}_1\text{-C}_3$ -alkylheteroaryl ;

$\text{R}^2$ ,  $\text{R}^3$  and  $\text{R}^5$  are H;

$\text{R}^8$  is  $\text{C}_1\text{-C}_4$ -alkylaryl

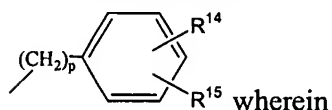
$\text{R}^9$  is chosen from hydrogen, alkyl, substituted alkyl,  $(\text{C}_1\text{-C}_4)$ -alkoxy,  $\text{C}_1\text{-C}_4$ -alkylcycloalkyl,  $\text{C}_1\text{-C}_4$ -alkylaryl, heterocyclyl,  $\text{C}_1\text{-C}_4$ -alkylheteroaryl,  $\text{C}_1\text{-C}_4$ -alkylheterocyclyl; and

m and n are zero.

33. (original) A 4-pyrimidinamine according to claim 32 wherein W is  $\text{NHR}^9$  and



$R^9$  is chosen from hydrogen; methyl; ethyl; 2,2,2-trifluoroethyl; allyl; cyclopropyl; 2-cyanoethyl; propargyl; methoxy; methoxyethyl; cyclopropyl; cyclopropylmethyl; (methylthio)ethyl; 3-methoxypropyl; 3-pyridyl; 2-(3-pyridyl)ethyl; 2-(2-pyridyl)ethyl; 3-pyridylmethyl; 4-pyridylmethyl; 4-pyridylmethyl-N-oxide; 2-pyridazinylmethyl; sulfolan-3-yl; 3-tetrahydrofuranyl; 2-tetrahydrofuranylmethyl; 3-(1-imidazolyl)propyl; 1-*t*-butoxycarbonyl-4-piperidyl; 1-*t*-butoxycarbonyl-4-piperidinylmethyl; 2-(hydroxyimino)propyl; 2-(methoxyimino)propyl; 2-oxo-1-propyl; and

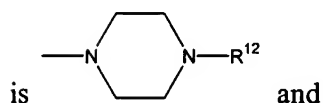


$R^{14}$  is chosen from H, Cl, F, CN, NO<sub>2</sub>, SO<sub>2</sub>NH<sub>2</sub>, CF<sub>3</sub>, COOCH<sub>3</sub>, OCH<sub>3</sub>, OH, SO<sub>2</sub>CH<sub>3</sub>, N(CH<sub>3</sub>)<sub>2</sub> and COOH;

$R^{15}$  is chosen from H, OCH<sub>3</sub> and Cl; and

$p$  is 1 or 2.

34. (original) A 4-pyrimidinamine according to claim 32 wherein W

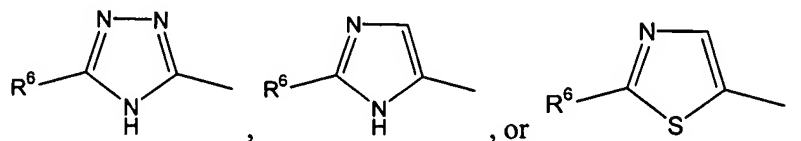


$R^{12}$  is *t*-butoxycarbonyl, methoxyacetyl or phenyl.

35. (currently amended) A 4-pyrimidinamine according to claim 28 wherein

Z is CH;

A is



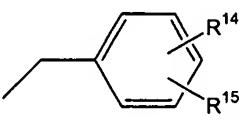
$R^1$  is chosen from *n*-butyl; cyclohexylmethyl; cyclopentylmethyl; 2-methylpropyl; 3-methyl-1-butyl; cyclohexyl; 2,2-dimethylpropyl; benzyl; 2-thienylmethyl; 1-

*t*-butoxycarbonyl-4-piperidinyl; 4-chlorobenzyl; 2-pyranylmethyl; 4-pyranylmethyl; 4-pyranyl and 1,1-dimethylethyl;

R<sup>2</sup> and R<sup>3</sup> are H;

Q is pyrrolyl;

W is NHR<sup>9</sup>; and

R<sup>9</sup> is alkyl, cycloalkyl or  wherein

R<sup>14</sup> is chosen from H, Cl, F, CN, NO<sub>2</sub>, SO<sub>2</sub>NH<sub>2</sub>, CF<sub>3</sub>, COOCH<sub>3</sub>, OCH<sub>3</sub>, SO<sub>2</sub>CH<sub>3</sub>, N(CH<sub>3</sub>)<sub>2</sub> and COOH; and

R<sup>15</sup> is chosen from H, OCH<sub>3</sub> and Cl.

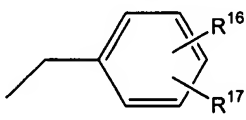
36. (currently amended) A pyrimidine according to claim 28 wherein:

A is R<sup>4</sup>R<sup>5</sup>N-C(O)-;

R<sup>1</sup> is chosen from isopropyl; n-butyl; cyclohexylmethyl; cyclopentylmethyl; naphthylmethyl; cyclohexylethyl; 2-methylpropyl; 3-methyl-1-butyl; cyclohexyl; 2,2-dimethylpropyl; benzyl; 2-thienylmethyl; 1-*t*-butoxycarbonyl-4-piperidinyl; 4-methoxybenzyl; 4-chlorobenzyl; 3,4-dichlorobenzyl; 2-pyranylmethyl; 4-pyranylmethyl; 4-pyranyl and 1,1-dimethylethyl;

R<sup>2</sup>, R<sup>3</sup> and R<sup>5</sup> are H;

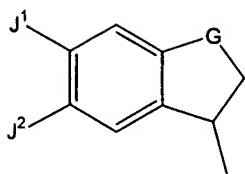
R<sup>4</sup> is pyridinyl, pyridinylmethyl, indanylmethyl, furanylmethyl, tetrahydronaphthalenyl,

substituted phenyl, or ;

R<sup>16</sup> is chosen from H, Cl, F, CN, NO<sub>2</sub>, SO<sub>2</sub>NH<sub>2</sub>, CF<sub>3</sub>, CH<sub>3</sub>, COOCH<sub>3</sub>, OCH<sub>3</sub>, SO<sub>2</sub>CH<sub>3</sub>, N(CH<sub>3</sub>)<sub>2</sub> and COOH; and

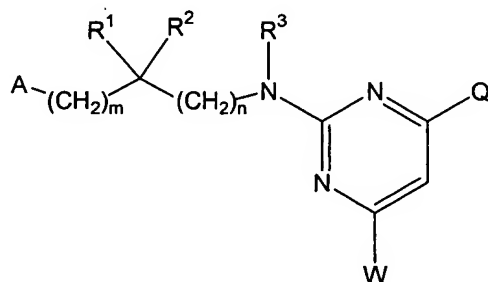
R<sup>17</sup> is chosen from H, OCH<sub>3</sub>, F and Cl.

37. (previously amended) A pyrimidine according to claim 28 wherein R<sup>4</sup> is



38. (original) A pyrimidine according to claim 37 wherein one of J<sup>1</sup> and J<sup>2</sup> is H and the other is H, Cl or CN and G is chosen from -CH<sub>2</sub>-, -CH<sub>2</sub>CH<sub>2</sub>-, -OCH<sub>2</sub>-, -O- and -CH<sub>2</sub>N(lower alkyl)-.

39. (previously amended) A 2-pyrimidinamine according to claim 28, wherein Y is CH, having the formula



40. (original) A 2-pyrimidinamine according to claim 39 wherein Q is chosen from pyrrolyl, pyridinyl, fluorophenyl and 2-thienyl.

41. (original) A 2-pyrimidinamine according to claim 40 wherein

A is R<sup>4</sup>R<sup>5</sup>N-C(O)-;

W is H, Cl, NHR<sup>9</sup> or OR<sup>8</sup>;

R<sup>1</sup> is chosen from alkyl and C<sub>1</sub>-C<sub>3</sub>-alkylcycloalkyl;

R<sup>2</sup>, R<sup>3</sup> and R<sup>5</sup> are H;

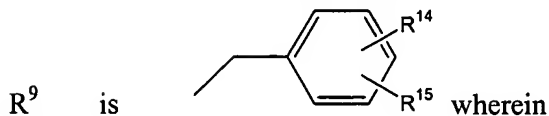
R<sup>4</sup> is C<sub>1</sub>-C<sub>4</sub>-alkylaryl or C<sub>1</sub>-C<sub>4</sub>-alkylheteroaryl;

R<sup>8</sup> is C<sub>1</sub>-C<sub>4</sub>-alkylaryl;

R<sup>9</sup> is chosen from hydrogen, alkyl, fluoroalkyl, (C<sub>1</sub>-C<sub>4</sub>-alkoxy)alkyl, (C<sub>1</sub>-C<sub>4</sub>-alkylthio)alkyl, C<sub>1</sub>-C<sub>4</sub>-alkylcycloalkyl, C<sub>1</sub>-C<sub>4</sub>-alkylaryl, heterocyclyl, C<sub>1</sub>-C<sub>4</sub>-alkylheteroaryl, C<sub>1</sub>-C<sub>4</sub>-alkylheterocyclyl; and

m and n are zero.

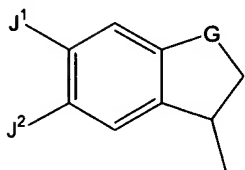
42. (original) A 2-pyrimidinamine according to claim 41 wherein W is  $\text{NHR}^9$  and



$\text{R}^{14}$  is chosen from H, F, Cl, CN,  $\text{NO}_2$ ,  $\text{SO}_2\text{NH}_2$ ,  $\text{CF}_3$ ,  $\text{COOCH}_3$ ,  $\text{OCH}_3$ ,  $\text{SO}_2\text{CH}_3$ ,  $\text{N}(\text{CH}_3)_2$  and  $\text{COOH}$ ; and

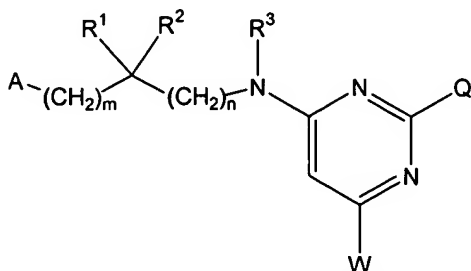
$\text{R}^{15}$  is chosen from H,  $\text{OCH}_3$  and Cl.

43. (original) A 2-pyrimidineamine according to claim 39 wherein  $\text{R}^4$  is



, one of  $\text{J}^1$  and  $\text{J}^2$  is H and the other is H, Cl or CN and G is chosen from  $-\text{CH}_2-$ ,  $-\text{CH}_2\text{CH}_2-$ ,  $-\text{OCH}_2-$ ,  $-\text{O}-$  and  $-\text{CH}_2\text{N}(\text{lower alkyl})-$ .

44. (previously amended) A 4-pyrimidinamine according to claim 28, wherein X is CH, having the formula



45. (original) A 4-pyrimidinamine according to claim 44 wherein Q is pyrrolyl and m and n are zero.

46. (original) A 4-pyrimidinamine according to claim 45 wherein:

A is  $\text{R}^4\text{R}^5\text{N}-\text{C}(\text{O})-$ ;

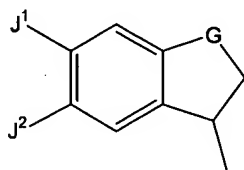
W is  $\text{NHR}^9$ ;

$\text{R}^1$  is chosen from cyclohexylmethyl; 2-methylpropyl and 3-methyl-1-butyl;

$\text{R}^2$ ,  $\text{R}^3$  and  $\text{R}^5$  are H; and

R<sup>4</sup> and R<sup>9</sup> are benzyl or substituted benzyl.

47. (original) A 4-pyrimidineamine according to claim 44 wherein R<sup>4</sup> is



, one of J<sup>1</sup> and J<sup>2</sup> is H and the other is H, Cl or CN and G is chosen from -CH<sub>2</sub>-, -CH<sub>2</sub>CH<sub>2</sub>-, -OCH<sub>2</sub>-, -O- and -CH<sub>2</sub>N(lower alkyl)-.

48. (currently amended) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound according to ~~claim 4~~ any of claims 4, 9, 12, or 26.

49. (original) A pharmaceutical composition according to claim 48 additionally comprising a steroidal or nonsteroidal antiinflammatory drug (NSAID).

50-51. (canceled)

52. (original) A pharmaceutical composition according to claim 48 additionally comprising a cyclooxygenase inhibitor.

53. (canceled)

54. (original) A pharmaceutical composition according to claim 48 additionally comprising a selective cyclooxygenase-2 inhibitor.

55. (canceled)

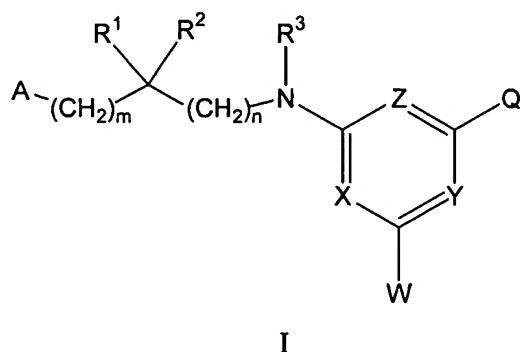
56. (original) A pharmaceutical composition according to claim 48 additionally comprising a selective cyclooxygenase-1 inhibitor.

57-58. (canceled)

59. (original) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound according to claim 28.
60. (original) A pharmaceutical composition according to claim 59 additionally comprising a steroidal or nonsteroidal antiinflammatory drug (NSAID).
61. (original) A pharmaceutical composition according to claim 59 additionally comprising a nonsteroidal antiinflammatory drug (NSAID).
62. (original) A pharmaceutical composition according to claim 61 wherein said NSAID is chosen from arylpropionic acids, arylacetic acids, arylbutyric acids, fenamic acids, arylcarboxylic acids, pyrazoles, pyrazolones, salicylic acids; and oxicams.
63. (original) A pharmaceutical composition according to claim 59 additionally comprising a cyclooxygenase inhibitor.
64. (original) A pharmaceutical composition according to claim 63 wherein said cyclooxygenase inhibitor is ibuprofen or a salicylic acid derivative.
65. (original) A pharmaceutical composition according to claim 59 additionally comprising a selective cyclooxygenase-2 inhibitor.
66. (original) A pharmaceutical composition according to claim 65 wherein said selective cyclooxygenase-2 inhibitor is rofecoxib or celecoxib.
67. (original) A pharmaceutical composition according to claim 59 additionally comprising a selective cyclooxygenase-1 inhibitor.
68. (original) A pharmaceutical composition according to claim 59 additionally comprising a steroidal antiinflammatory drug.

69. (original) A pharmaceutical composition according to claim 68 wherein said steroidal antiinflammatory drug is chosen from finasteride, beclomethasone and hydrocortisone.

70. (currently amended) A method of treating vasculopathy ~~a condition resulting from inappropriate bradykinin receptor activity~~ comprising administering to a subject in need of such treatment a therapeutically effective amount of a compound of formula I

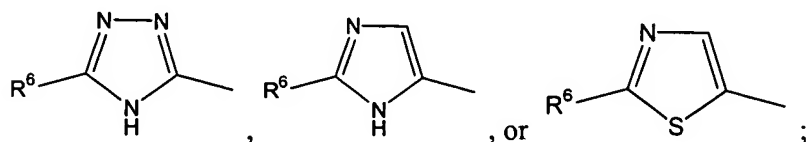


wherein:

two of X, Y and Z are N and the other of X, Y and Z is CH;

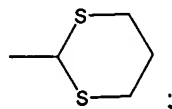
A is A<sup>1</sup> or A<sup>2</sup>;

A<sup>1</sup> is R<sup>4</sup>R<sup>5</sup>N-C(O)-,



A<sup>2</sup> is chosen from R<sup>7</sup>C(O)NH-, R<sup>7</sup>S(O)<sub>2</sub>NH-, R<sup>4</sup>NH-, and R<sup>4</sup>O-;

Q is chosen from heteroaryl, aryl, -CH<sub>2</sub>R<sup>13</sup>, -CH=N-OCH<sub>3</sub> and



W is chosen from H, Cl, F, R<sup>8</sup>, C<sub>1</sub>-C<sub>4</sub>-alkylaryl, -OR<sup>8</sup>, -SR<sup>8</sup>, -NR<sup>9</sup>R<sup>10</sup> and -NHC(O)R<sup>11</sup>, with the proviso that when Q is imidazolyl, W is not ~~may not be~~ H, Cl, F or R<sup>8</sup>;

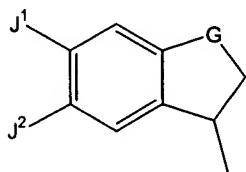
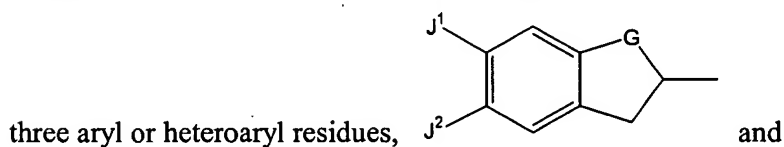
R<sup>1</sup> is chosen from alkyl, cycloalkyl, alkenyl, C<sub>1</sub>-C<sub>3</sub>-alkylcycloalkyl, heterocyclyl, C<sub>1</sub>-C<sub>3</sub>-alkylheterocyclyl, aryl, C<sub>1</sub>-C<sub>3</sub>-alkylaryl, heteroaryl,

C<sub>1</sub>-C<sub>3</sub>-alkylheteroaryl, (C<sub>1</sub>-C<sub>3</sub>-alkyloxy)alkyl, (C<sub>1</sub>-C<sub>3</sub>-alkyloxy)cycloalkyl, (C<sub>1</sub>-C<sub>3</sub>-alkylthio)alkyl, (C<sub>1</sub>-C<sub>3</sub>-alkylthio)cycloalkyl and (C<sub>1</sub>-C<sub>3</sub>-alkylsulfonyl)alkyl;

R<sup>2</sup> is H or C<sub>1</sub>-C<sub>3</sub>-alkyl, or R<sup>1</sup> and R<sup>2</sup> taken together form a 5- to 7-membered ring structure optionally containing O, S or NR<sup>12</sup>;

R<sup>3</sup> is H or C<sub>1</sub>-C<sub>6</sub>-alkyl, or, when n is zero, R<sup>2</sup> and R<sup>3</sup> taken together may form a 6-membered ring, which may be fused to a six-membered saturated or aromatic carbocycle;

R<sup>4</sup> is chosen from H, aryl, heteroaryl, C<sub>1</sub>-C<sub>4</sub>-alkyl substituted with from one to



, wherein J<sup>1</sup> and J<sup>2</sup> are independently chosen from H,

F, Cl, CN, NO<sub>2</sub> and CH<sub>3</sub>, and G is chosen from -CH<sub>2</sub>-, -CH<sub>2</sub>CH<sub>2</sub>-, -CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>-, -OCH<sub>2</sub>-, -CH<sub>2</sub>O-, -CH<sub>2</sub>CH<sub>2</sub>O-, -OCH<sub>2</sub>CH<sub>2</sub>-, -O-, -N(lower alkyl)-, -N(lower alkyl)CH<sub>2</sub>-, -CH<sub>2</sub>N(lower alkyl)-, -S-, -SO-, -SO<sub>2</sub>-, -CH<sub>2</sub>S-, -SCH<sub>2</sub>-, -CH<sub>2</sub>SO-, -SOCH<sub>2</sub>-, -CH<sub>2</sub>SO<sub>2</sub>-, and -SO<sub>2</sub>CH<sub>2</sub>-;

R<sup>5</sup> is H or C<sub>1</sub>-C<sub>3</sub>-alkyl, with the proviso that both R<sup>3</sup> and R<sup>5</sup> cannot be alkyl;

R<sup>6</sup> is aryl;

R<sup>7</sup> is aryl or C<sub>1</sub>-C<sub>3</sub>-alkylaryl;

R<sup>8</sup> is chosen from alkyl, aryl, heteroaryl, substituted alkyl, C<sub>1</sub>-C<sub>4</sub>-alkylaryl, C<sub>1</sub>-C<sub>4</sub>-alkylheterocyclyl and C<sub>1</sub>-C<sub>4</sub>-alkylheteroaryl;

R<sup>9</sup> is chosen from H, alkyl, alkenyl, substituted alkyl, cycloalkyl, aryl, alkoxy, heteroaryl, fluoroalkyl, C<sub>1</sub>-C<sub>4</sub>-alkylcycloalkyl, (C<sub>1</sub>-C<sub>4</sub>-alkoxy)alkyl, (C<sub>1</sub>-C<sub>4</sub>-alkoxycarbonyl)alkyl, (C<sub>1</sub>-C<sub>4</sub>-alkylthio)alkyl, heterocyclyl, C<sub>1</sub>-C<sub>4</sub>-alkylheterocyclyl, C<sub>1</sub>-C<sub>4</sub>-alkylaryl, and C<sub>1</sub>-C<sub>4</sub>-alkylheteroaryl;

R<sup>10</sup> is H or C<sub>1</sub>-C<sub>3</sub>-alkyl, or

R<sup>9</sup> and R<sup>10</sup> taken together may form a 5- to 7-membered ring structure optionally



containing O, S, SO, SO<sub>2</sub> or NR<sup>12</sup>, said ring optionally substituted with  
-OH, -CN, -COOH or -COOCH<sub>3</sub>;

R<sup>11</sup> is aryl;

R<sup>12</sup> is chosen from H, C<sub>1</sub>-C<sub>3</sub>-alkyl, alkoxycarbonyl, methoxyacetyl and aryl;

R<sup>13</sup> is chosen from -OH, -OTHP, 1-imidazolyl, and 1-pyrrolyl;

m is zero or one; and

n is zero or one, with the proviso that when A is A<sup>2</sup>, m and n cannot both be  
zero.

71. (canceled)

72. (currently amended) The method according to claim 70 wherein said ~~condition~~  
~~resulting from inappropriate bradykinin receptor activity~~ vasculopathy is diabetic  
vasculopathy, ~~post-capillary resistance or diabetic symptoms associated with insulinitis.~~

73. (currently amended) The method according to claim 100 ~~72~~ wherein said diabetic  
symptoms associated with insulinitis comprise hyperglycemia, diuresis, proteinuria and  
increased nitrile and kallikrein urinary excretion.

74-75. (canceled)

76. (currently amended) The method according to claim 99 ~~75~~ wherein said pain is  
chronic pain, pain associated with inflammation or dental pain.

77. (currently amended) The method of treating pain or hyperalgesia according to claim  
99 ~~75~~ additionally comprising administering a steroidal or nonsteroidal antiinflammatory  
drug (NSAID).

78. (original) The method of treating pain or hyperalgesia according to claim 77 wherein  
an NSAID is administered.

79. (currently amended) The method of treating pain or hyperalgesia according to claim ~~99~~ 75 additionally comprising administering a cyclooxygenase inhibitor.

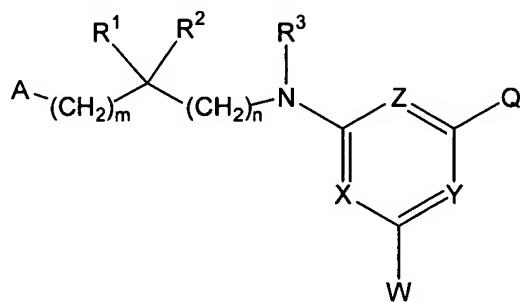
80. (original) The method of treating pain or hyperalgesia according to claim 79 wherein said cyclooxygenase inhibitor is a selective cyclooxygenase-2 inhibitor.

81. (original) The method of treating pain or hyperalgesia according to claim 79 wherein said cyclooxygenase inhibitor is a selective cyclooxygenase-1 inhibitor.

82-94. (canceled)

95. (new) The method according to claim 70 wherein said vasculopathy is hypertensive vasculopathy.

96. (new) A method of treating asthma comprising administering to a subject in need of such treatment a therapeutically effective amount of a compound of formula I



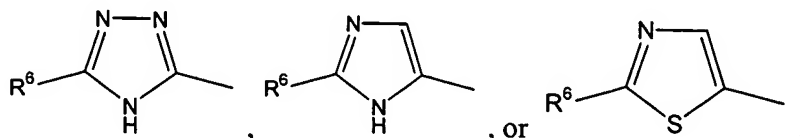
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wherein:

two of X, Y and Z are N and the other of X, Y and Z is CH;

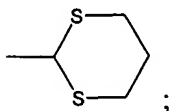
A is A<sup>1</sup> or A<sup>2</sup>;

A<sup>1</sup> is R<sup>4</sup>R<sup>5</sup>N-C(O)-,



$A^2$  is chosen from  $R^7C(O)NH-$ ,  $R^7S(O)_2NH-$ ,  $R^4NH-$ , and  $R^4O-$ ;

Q is chosen from heteroaryl, aryl,  $-CH_2R^{13}$ ,  $-CH=N-OCH_3$  and



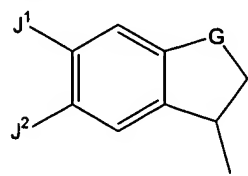
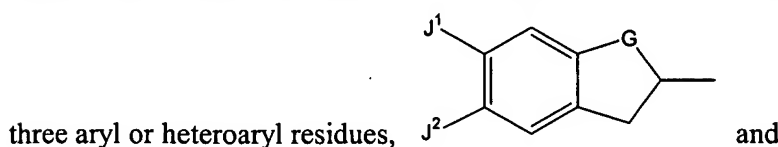
W is chosen from H, Cl, F,  $R^8$ ,  $C_1-C_4$ -alkylaryl,  $-OR^8$ ,  $-SR^8$ ,  $-NR^9R^{10}$  and  $-NHC(O)R^{11}$ , with the proviso that when Q is imidazolyl, W is not H, Cl, F or  $R^8$ ;

$R^1$  is chosen from alkyl, cycloalkyl, alkenyl,  $C_1-C_3$ -alkylcycloalkyl, heterocyclyl,  $C_1-C_3$ -alkylheterocyclyl, aryl,  $C_1-C_3$ -alkylaryl, heteroaryl,  $C_1-C_3$ -alkylheteroaryl,  $(C_1-C_3$ -alkyloxy)alkyl,  $(C_1-C_3$ -alkyloxy)cycloalkyl,  $(C_1-C_3$ -alkylthio)alkyl,  $(C_1-C_3$ -alkylthio)cycloalkyl and  $(C_1-C_3$ -alkylsulfonyl)alkyl;

$R^2$  is H or  $C_1-C_3$ -alkyl, or  $R^1$  and  $R^2$  taken together form a 5- to 7-membered ring structure optionally containing O, S or  $NR^{12}$ ;

$R^3$  is H or  $C_1-C_6$ -alkyl, or, when n is zero,  $R^2$  and  $R^3$  taken together may form a 6-membered ring, which may be fused to a six-membered saturated or aromatic carbocycle;

$R^4$  is chosen from H, aryl, heteroaryl,  $C_1-C_4$ -alkyl substituted with from one to

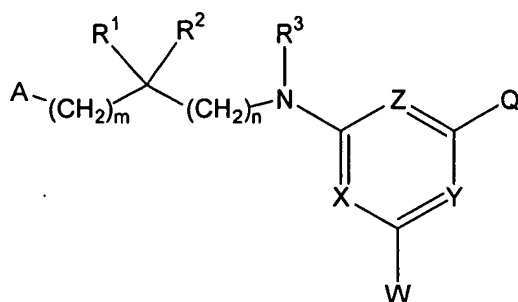


, wherein  $J^1$  and  $J^2$  are independently chosen from H, F, Cl, CN,  $NO_2$  and  $CH_3$ , and G is chosen from  $-CH_2-$ ,  $-CH_2CH_2-$ ,  $-CH_2CH_2CH_2-$ ,  $-OCH_2-$ ,  $-CH_2O-$ ,  $-CH_2CH_2O-$ ,  $-OCH_2CH_2-$ ,  $-O-$ ,  $-N$ (lower alkyl)-,  $-N$ (lower alkyl) $CH_2-$ ,  $-CH_2N$ (lower alkyl)-,  $-S-$ ,  $-SO-$ ,  $-SO_2-$ ,  $-CH_2S-$ ,  $-SCH_2-$ ,  $-CH_2SO-$ ,  $-SOCH_2-$ ,  $-CH_2SO_2-$ , and  $-SO_2CH_2-$ ;

$R^5$  is H or  $C_1-C_3$ -alkyl, with the proviso that both  $R^3$  and  $R^5$  cannot be alkyl;

- $R^6$  is aryl;  
 $R^7$  is aryl or  $C_1$ - $C_3$ -alkylaryl;  
 $R^8$  is chosen from alkyl, aryl, heteroaryl, substituted alkyl,  $C_1$ - $C_4$ -alkylaryl,  $C_1$ - $C_4$ -alkylheterocyclyl and  $C_1$ - $C_4$ -alkylheteroaryl;  
 $R^9$  is chosen from H, alkyl, alkenyl, substituted alkyl, cycloalkyl, aryl, alkoxy, heteroaryl, fluoroalkyl,  $C_1$ - $C_4$ -alkylcycloalkyl, ( $C_1$ - $C_4$ -alkoxy)alkyl, ( $C_1$ - $C_4$ -alkoxycarbonyl)alkyl, ( $C_1$ - $C_4$ -alkylthio)alkyl, heterocyclyl,  $C_1$ - $C_4$ -alkylheterocyclyl,  $C_1$ - $C_4$ -alkylaryl, and  $C_1$ - $C_4$ -alkylheteroaryl;  
 $R^{10}$  is H or  $C_1$ - $C_3$ -alkyl, or  
 $R^9$  and  $R^{10}$  taken together may form a 5- to 7-membered ring structure optionally containing O, S, SO,  $SO_2$  or  $NR^{12}$ , said ring optionally substituted with -OH, -CN, -COOH or -COOCH<sub>3</sub>;  
 $R^{11}$  is aryl;  
 $R^{12}$  is chosen from H,  $C_1$ - $C_3$ -alkyl, alkoxycarbonyl, methoxyacetyl and aryl;  
 $R^{13}$  is chosen from -OH, -OTHP, 1-imidazolyl, and 1-pyrrolyl;  
 m is zero or one; and  
 n is zero or one, with the proviso that when A is  $A^2$ , m and n cannot both be zero.

97. (new) A method of treating inflammation comprising administering to a subject in need of such treatment a therapeutically effective amount of a compound of formula I



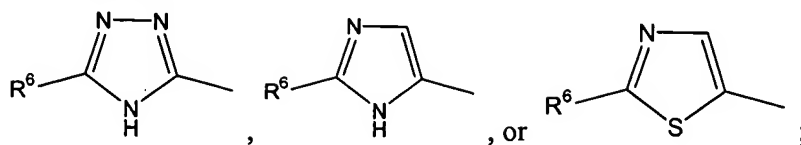
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wherein:

two of X, Y and Z are N and the other of X, Y and Z is CH;

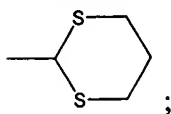
A is  $A^1$  or  $A^2$ ;

$A^1$  is  $R^4R^5N-C(O)-$ ,



$A^2$  is chosen from  $R^7C(O)NH-$ ,  $R^7S(O)_2NH-$ ,  $R^4NH-$ , and  $R^4O-$ ;

Q is chosen from heteroaryl, aryl,  $-CH_2R^{13}$ ,  $-CH=N-OCH_3$  and



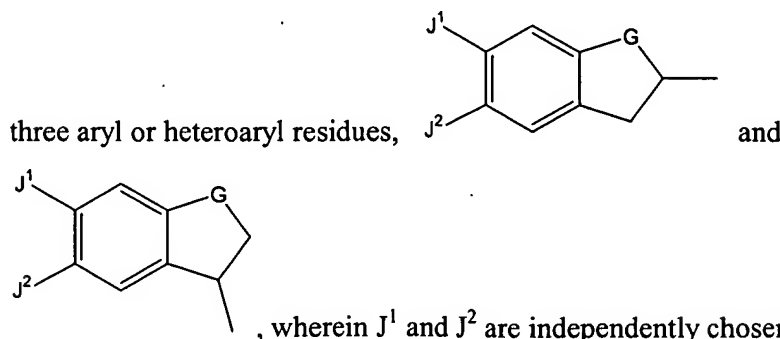
W is chosen from H, Cl, F,  $R^8$ ,  $C_1-C_4$ -alkylaryl,  $-OR^8$ ,  $-SR^8$ ,  $-NR^9R^{10}$  and  $-NHC(O)R^{11}$ , with the proviso that when Q is imidazolyl, W is not H, Cl, F or  $R^8$ ;

$R^1$  is chosen from alkyl, cycloalkyl, alkenyl,  $C_1-C_3$ -alkylcycloalkyl, heterocyclyl,  $C_1-C_3$ -alkylheterocyclyl, aryl,  $C_1-C_3$ -alkylaryl, heteroaryl,  $C_1-C_3$ -alkylheteroaryl,  $(C_1-C_3$ -alkyloxy)alkyl,  $(C_1-C_3$ -alkyloxy)cycloalkyl,  $(C_1-C_3$ -alkylthio)alkyl,  $(C_1-C_3$ -alkylthio)cycloalkyl and  $(C_1-C_3$ -alkylsulfonyl)alkyl;

$R^2$  is H or  $C_1-C_3$ -alkyl, or  $R^1$  and  $R^2$  taken together form a 5- to 7-membered ring structure optionally containing O, S or  $NR^{12}$ ;

$R^3$  is H or  $C_1-C_6$ -alkyl, or, when n is zero,  $R^2$  and  $R^3$  taken together may form a 6-membered ring, which may be fused to a six-membered saturated or aromatic carbocycle;

$R^4$  is chosen from H, aryl, heteroaryl,  $C_1-C_4$ -alkyl substituted with from one to



F, Cl, CN,  $NO_2$  and  $CH_3$ , and G is chosen from  $-CH_2-$ ,  $-CH_2CH_2-$ ,

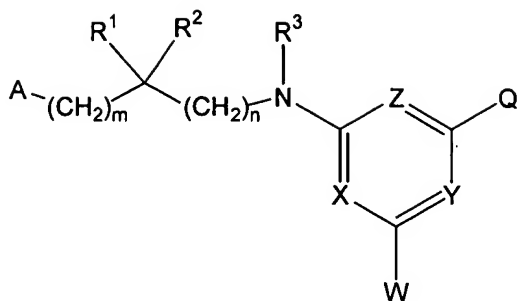
-CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>-, -OCH<sub>2</sub>-, -CH<sub>2</sub>O-, -CH<sub>2</sub>CH<sub>2</sub>O-, -OCH<sub>2</sub>CH<sub>2</sub>-, -O-, -N(lower alkyl)-, -N(lower alkyl)CH<sub>2</sub>-, -CH<sub>2</sub>N(lower alkyl)-, -S-, -SO-, -SO<sub>2</sub>-,  
-CH<sub>2</sub>S-, -SCH<sub>2</sub>-, -CH<sub>2</sub>SO-, -SOCH<sub>2</sub>-, -CH<sub>2</sub>SO<sub>2</sub>-, and -SO<sub>2</sub>CH<sub>2</sub>-;

- R<sup>5</sup> is H or C<sub>1</sub>-C<sub>3</sub>-alkyl, with the proviso that both R<sup>3</sup> and R<sup>5</sup> cannot be alkyl;
- R<sup>6</sup> is aryl;
- R<sup>7</sup> is aryl or C<sub>1</sub>-C<sub>3</sub>-alkylaryl;
- R<sup>8</sup> is chosen from alkyl, aryl, heteroaryl, substituted alkyl, C<sub>1</sub>-C<sub>4</sub>-alkylaryl, C<sub>1</sub>-C<sub>4</sub>-alkylheterocyclyl and C<sub>1</sub>-C<sub>4</sub>-alkylheteroaryl;
- R<sup>9</sup> is chosen from H, alkyl, alkenyl, substituted alkyl, cycloalkyl, aryl, alkoxy, heteroaryl, fluoroalkyl, C<sub>1</sub>-C<sub>4</sub>-alkylcycloalkyl, (C<sub>1</sub>-C<sub>4</sub>-alkoxy)alkyl, (C<sub>1</sub>-C<sub>4</sub>-alkoxycarbonyl)alkyl, (C<sub>1</sub>-C<sub>4</sub>-alkylthio)alkyl, heterocyclyl, C<sub>1</sub>-C<sub>4</sub>-alkylheterocyclyl, C<sub>1</sub>-C<sub>4</sub>-alkylaryl, and C<sub>1</sub>-C<sub>4</sub>-alkylheteroaryl;
- R<sup>10</sup> is H or C<sub>1</sub>-C<sub>3</sub>-alkyl, or
- R<sup>9</sup> and R<sup>10</sup> taken together may form a 5- to 7-membered ring structure optionally containing O, S, SO, SO<sub>2</sub> or NR<sup>12</sup>, said ring optionally substituted with -OH, -CN, -COOH or -COOCH<sub>3</sub>;
- R<sup>11</sup> is aryl;
- R<sup>12</sup> is chosen from H, C<sub>1</sub>-C<sub>3</sub>-alkyl, alkoxycarbonyl, methoxyacetyl and aryl;
- R<sup>13</sup> is chosen from -OH, -OTHP, 1-imidazolyl, and 1-pyrrolyl;
- m is zero or one; and
- n is zero or one, with the proviso that when A is A<sup>2</sup>, m and n cannot both be zero.

98. (new) The method of claim 97 wherein said inflammation is associated with edema, rhinitis, septic shock, multiple sclerosis, atherosclerosis, Alzheimer's disease, or closed head trauma.

99. (new) A method of treating pain or hyperalgesia comprising administering to a subject in need of such treatment a therapeutically effective amount of a compound of

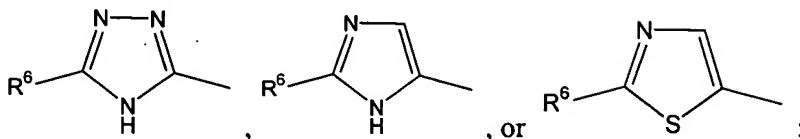
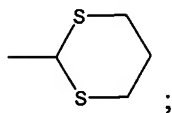
formula I



I

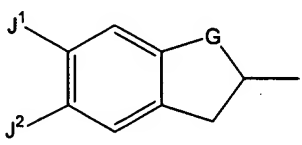
wherein:

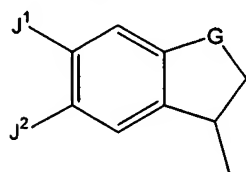
two of X, Y and Z are N and the other of X, Y and Z is CH;

A is A<sup>1</sup> or A<sup>2</sup>;A<sup>1</sup> is R<sup>4</sup>R<sup>5</sup>N-C(O)-,A<sup>2</sup> is chosen from R<sup>7</sup>C(O)NH-, R<sup>7</sup>S(O)<sub>2</sub>NH-, R<sup>4</sup>NH-, and R<sup>4</sup>O-;Q is chosen from heteroaryl, aryl, -CH<sub>2</sub>R<sup>13</sup>, -CH=N-OCH<sub>3</sub> andW is chosen from H, Cl, F, R<sup>8</sup>, C<sub>1</sub>-C<sub>4</sub>-alkylaryl, -OR<sup>8</sup>, -SR<sup>8</sup>, -NR<sup>9</sup>R<sup>10</sup> and -NHC(O)R<sup>11</sup>, with the proviso that when Q is imidazolyl, W is not H, Cl, F or R<sup>8</sup>;R<sup>1</sup> is chosen from alkyl, cycloalkyl, alkenyl, C<sub>1</sub>-C<sub>3</sub>-alkylcycloalkyl, heterocyclyl, C<sub>1</sub>-C<sub>3</sub>-alkylheterocyclyl, aryl, C<sub>1</sub>-C<sub>3</sub>-alkylaryl, heteroaryl, C<sub>1</sub>-C<sub>3</sub>-alkylheteroaryl, (C<sub>1</sub>-C<sub>3</sub>-alkyloxy)alkyl, (C<sub>1</sub>-C<sub>3</sub>-alkyloxy)cycloalkyl, (C<sub>1</sub>-C<sub>3</sub>-alkylthio)alkyl, (C<sub>1</sub>-C<sub>3</sub>-alkylthio)cycloalkyl and (C<sub>1</sub>-C<sub>3</sub>-alkylsulfonyl)alkyl;R<sup>2</sup> is H or C<sub>1</sub>-C<sub>3</sub>-alkyl, or R<sup>1</sup> and R<sup>2</sup> taken together form a 5- to 7-membered ring structure optionally containing O, S or NR<sup>12</sup>;R<sup>3</sup> is H or C<sub>1</sub>-C<sub>6</sub>-alkyl, or, when n is zero, R<sup>2</sup> and R<sup>3</sup> taken together may form

a 6-membered ring, which may be fused to a six-membered saturated or aromatic carbocycle;

R<sup>4</sup> is chosen from H, aryl, heteroaryl, C<sub>1</sub>-C<sub>4</sub>-alkyl substituted with from one to

three aryl or heteroaryl residues,  and



, wherein J<sup>1</sup> and J<sup>2</sup> are independently chosen from H,

F, Cl, CN, NO<sub>2</sub> and CH<sub>3</sub>, and G is chosen from -CH<sub>2</sub>-, -CH<sub>2</sub>CH<sub>2</sub>-,  
-CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>-, -OCH<sub>2</sub>-, -CH<sub>2</sub>O-, -CH<sub>2</sub>CH<sub>2</sub>O-, -OCH<sub>2</sub>CH<sub>2</sub>-, -O-, -N(lower  
alkyl)-, -N(lower alkyl)CH<sub>2</sub>-, -CH<sub>2</sub>N(lower alkyl)-, -S-, -SO-, -SO<sub>2</sub>-,  
-CH<sub>2</sub>S-, -SCH<sub>2</sub>-, -CH<sub>2</sub>SO-, -SOCH<sub>2</sub>-, -CH<sub>2</sub>SO<sub>2</sub>-, and -SO<sub>2</sub>CH<sub>2</sub>-;

R<sup>5</sup> is H or C<sub>1</sub>-C<sub>3</sub>-alkyl, with the proviso that both R<sup>3</sup> and R<sup>5</sup> cannot be alkyl;

R<sup>6</sup> is aryl;

R<sup>7</sup> is aryl or C<sub>1</sub>-C<sub>3</sub>-alkylaryl;

R<sup>8</sup> is chosen from alkyl, aryl, heteroaryl, substituted alkyl, C<sub>1</sub>-C<sub>4</sub>-alkylaryl, C<sub>1</sub>-C<sub>4</sub>-alkylheterocyclyl and C<sub>1</sub>-C<sub>4</sub>-alkylheteroaryl;

R<sup>9</sup> is chosen from H, alkyl, alkenyl, substituted alkyl, cycloalkyl, aryl, alkoxy, heteroaryl, fluoroalkyl, C<sub>1</sub>-C<sub>4</sub>-alkylcycloalkyl, (C<sub>1</sub>-C<sub>4</sub>-alkoxy)alkyl, (C<sub>1</sub>-C<sub>4</sub>-alkoxycarbonyl)alkyl, (C<sub>1</sub>-C<sub>4</sub>-alkylthio)alkyl, heterocyclyl, C<sub>1</sub>-C<sub>4</sub>-alkylheterocyclyl, C<sub>1</sub>-C<sub>4</sub>-alkylaryl, and C<sub>1</sub>-C<sub>4</sub>-alkylheteroaryl;

R<sup>10</sup> is H or C<sub>1</sub>-C<sub>3</sub>-alkyl, or

R<sup>9</sup> and R<sup>10</sup> taken together may form a 5- to 7-membered ring structure optionally containing O, S, SO, SO<sub>2</sub> or NR<sup>12</sup>, said ring optionally substituted with -OH, -CN, -COOH or -COOCH<sub>3</sub>;

R<sup>11</sup> is aryl;

R<sup>12</sup> is chosen from H, C<sub>1</sub>-C<sub>3</sub>-alkyl, alkoxycarbonyl, methoxyacetyl and aryl;

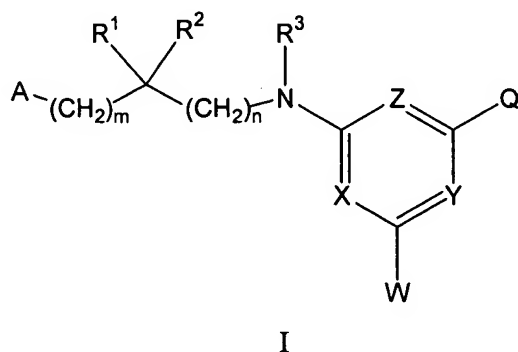
R<sup>13</sup> is chosen from -OH, -OTHP, 1-imidazolyl, and 1-pyrrolyl;

m is zero or one; and



n is zero or one, with the proviso that when A is A<sup>2</sup>, m and n cannot both be zero.

100. (new) A method of treating post-capillary resistance or diabetic symptoms associated with insulinitis comprising administering to a subject in need of such treatment a therapeutically effective amount of a compound of formula I

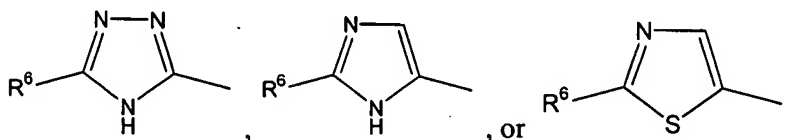


wherein:

two of X, Y and Z are N and the other of X, Y and Z is CH;

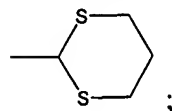
A is A<sup>1</sup> or A<sup>2</sup>;

A<sup>1</sup> is R<sup>4</sup>R<sup>5</sup>N-C(O)-,



A<sup>2</sup> is chosen from R<sup>7</sup>C(O)NH-, R<sup>7</sup>S(O)<sub>2</sub>NH-, R<sup>4</sup>NH-, and R<sup>4</sup>O-;

Q is chosen from heteroaryl, aryl, -CH<sub>2</sub>R<sup>13</sup>, -CH=N-OCH<sub>3</sub> and



W is chosen from H, Cl, F, R<sup>8</sup>, C<sub>1</sub>-C<sub>4</sub>-alkylaryl, -OR<sup>8</sup>, -SR<sup>8</sup>, -NR<sup>9</sup>R<sup>10</sup> and -NHC(O)R<sup>11</sup>, with the proviso that when Q is imidazolyl, W is not H, Cl, F or R<sup>8</sup>;

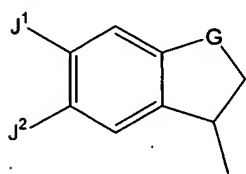
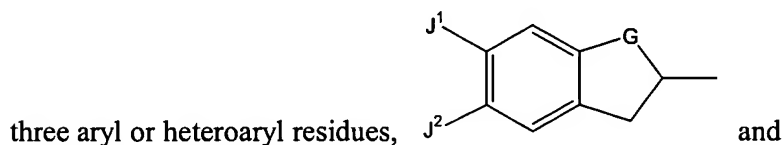
R<sup>1</sup> is chosen from alkyl, cycloalkyl, alkenyl, C<sub>1</sub>-C<sub>3</sub>-alkylcycloalkyl, heterocyclyl, C<sub>1</sub>-C<sub>3</sub>-alkylheterocyclyl, aryl, C<sub>1</sub>-C<sub>3</sub>-alkylaryl, heteroaryl,

C<sub>1</sub>-C<sub>3</sub>-alkylheteroaryl, (C<sub>1</sub>-C<sub>3</sub>-alkyloxy)alkyl, (C<sub>1</sub>-C<sub>3</sub>-alkyloxy)cycloalkyl, (C<sub>1</sub>-C<sub>3</sub>-alkylthio)alkyl, (C<sub>1</sub>-C<sub>3</sub>-alkylthio)cycloalkyl and (C<sub>1</sub>-C<sub>3</sub>-alkylsulfonyl)alkyl;

R<sup>2</sup> is H or C<sub>1</sub>-C<sub>3</sub>-alkyl, or R<sup>1</sup> and R<sup>2</sup> taken together form a 5- to 7-membered ring structure optionally containing O, S or NR<sup>12</sup>;

R<sup>3</sup> is H or C<sub>1</sub>-C<sub>6</sub>-alkyl, or, when n is zero, R<sup>2</sup> and R<sup>3</sup> taken together may form a 6-membered ring, which may be fused to a six-membered saturated or aromatic carbocycle;

R<sup>4</sup> is chosen from H, aryl, heteroaryl, C<sub>1</sub>-C<sub>4</sub>-alkyl substituted with from one to



, wherein J<sup>1</sup> and J<sup>2</sup> are independently chosen from H, F, Cl, CN, NO<sub>2</sub> and CH<sub>3</sub>, and G is chosen from -CH<sub>2</sub>-, -CH<sub>2</sub>CH<sub>2</sub>-, -CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>-, -OCH<sub>2</sub>-, -CH<sub>2</sub>O-, -CH<sub>2</sub>CH<sub>2</sub>O-, -OCH<sub>2</sub>CH<sub>2</sub>-, -O-, -N(lower alkyl)-, -N(lower alkyl)CH<sub>2</sub>-, -CH<sub>2</sub>N(lower alkyl)-, -S-, -SO-, -SO<sub>2</sub>-, -CH<sub>2</sub>S-, -SCH<sub>2</sub>-, -CH<sub>2</sub>SO-, -SOCH<sub>2</sub>-, -CH<sub>2</sub>SO<sub>2</sub>-, and -SO<sub>2</sub>CH<sub>2</sub>-;

R<sup>5</sup> is H or C<sub>1</sub>-C<sub>3</sub>-alkyl, with the proviso that both R<sup>3</sup> and R<sup>5</sup> cannot be alkyl;

R<sup>6</sup> is aryl;

R<sup>7</sup> is aryl or C<sub>1</sub>-C<sub>3</sub>-alkylaryl;

R<sup>8</sup> is chosen from alkyl, aryl, heteroaryl, substituted alkyl, C<sub>1</sub>-C<sub>4</sub>-alkylaryl, C<sub>1</sub>-C<sub>4</sub>-alkylheterocyclyl and C<sub>1</sub>-C<sub>4</sub>-alkylheteroaryl;

R<sup>9</sup> is chosen from H, alkyl, alkenyl, substituted alkyl, cycloalkyl, aryl, alkoxy, heteroaryl, fluoroalkyl, C<sub>1</sub>-C<sub>4</sub>-alkylcycloalkyl, (C<sub>1</sub>-C<sub>4</sub>-alkoxy)alkyl, (C<sub>1</sub>-C<sub>4</sub>-alkoxycarbonyl)alkyl, (C<sub>1</sub>-C<sub>4</sub>-alkylthio)alkyl, heterocyclyl, C<sub>1</sub>-C<sub>4</sub>-alkylheterocyclyl, C<sub>1</sub>-C<sub>4</sub>-alkylaryl, and C<sub>1</sub>-C<sub>4</sub>-alkylheteroaryl;

R<sup>10</sup> is H or C<sub>1</sub>-C<sub>3</sub>-alkyl, or

$R^9$  and  $R^{10}$  taken together may form a 5- to 7-membered ring structure optionally containing O, S, SO,  $SO_2$  or  $NR^{12}$ , said ring optionally substituted with -OH, -CN, -COOH or -COOCH<sub>3</sub>;

$R^{11}$  is aryl;

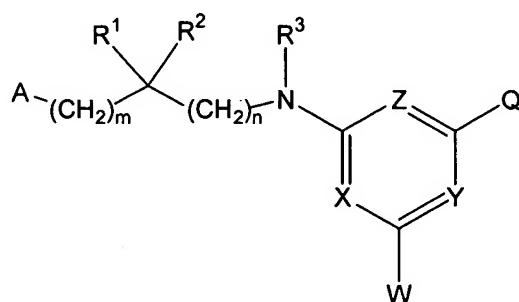
$R^{12}$  is chosen from H, C<sub>1</sub>-C<sub>3</sub>-alkyl, alkoxycarbonyl, methoxyacetyl and aryl;

$R^{13}$  is chosen from -OH, -OTHP, 1-imidazolyl, and 1-pyrrolyl;

m is zero or one; and

n is zero or one, with the proviso that when A is A<sup>2</sup>, m and n cannot both be zero.

101. (new) A method of treating edema comprising administering to a subject in need of such treatment a therapeutically effective amount of a compound of formula I



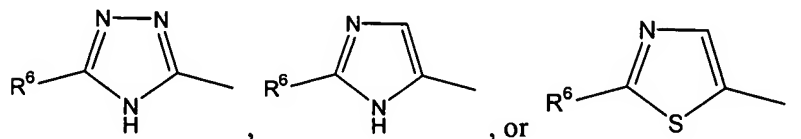
I

wherein:

two of X, Y and Z are N and the other of X, Y and Z is CH;

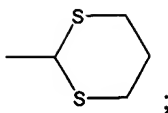
A is A<sup>1</sup> or A<sup>2</sup>;

A<sup>1</sup> is  $R^4R^5N-C(O)-$ ,



A<sup>2</sup> is chosen from  $R^7C(O)NH-$ ,  $R^7S(O)_2NH-$ ,  $R^4NH-$ , and  $R^4O-$ ;

Q is chosen from heteroaryl, aryl,  $-CH_2R^{13}$ ,  $-CH=N-OCH_3$  and



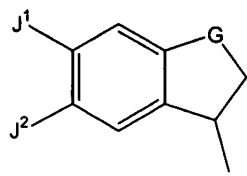
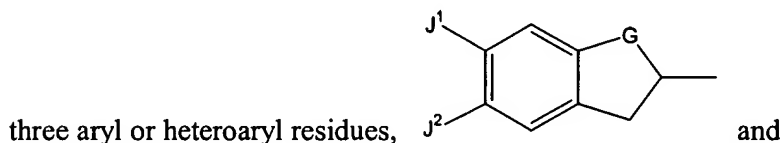
W is chosen from H, Cl, F,  $R^8$ ,  $C_1$ - $C_4$ -alkylaryl,  $-OR^8$ ,  $-SR^8$ ,  $-NR^9R^{10}$  and  $-NHC(O)R^{11}$ , with the proviso that when Q is imidazolyl, W is not H, Cl, F or  $R^8$ ;

$R^1$  is chosen from alkyl, cycloalkyl, alkenyl,  $C_1$ - $C_3$ -alkylcycloalkyl, heterocyclyl,  $C_1$ - $C_3$ -alkylheterocyclyl, aryl,  $C_1$ - $C_3$ -alkylaryl, heteroaryl,  $C_1$ - $C_3$ -alkylheteroaryl,  $(C_1$ - $C_3$ -alkyloxy)alkyl,  $(C_1$ - $C_3$ -alkyloxy)cycloalkyl,  $(C_1$ - $C_3$ -alkylthio)alkyl,  $(C_1$ - $C_3$ -alkylthio)cycloalkyl and  $(C_1$ - $C_3$ -alkylsulfonyl)alkyl;

$R^2$  is H or  $C_1$ - $C_3$ -alkyl, or  $R^1$  and  $R^2$  taken together form a 5- to 7-membered ring structure optionally containing O, S or  $NR^{12}$ ;

$R^3$  is H or  $C_1$ - $C_6$ -alkyl, or, when n is zero,  $R^2$  and  $R^3$  taken together may form a 6-membered ring, which may be fused to a six-membered saturated or aromatic carbocycle;

$R^4$  is chosen from H, aryl, heteroaryl,  $C_1$ - $C_4$ -alkyl substituted with from one to



, wherein  $J^1$  and  $J^2$  are independently chosen from H, F, Cl, CN,  $NO_2$  and  $CH_3$ , and G is chosen from  $-CH_2-$ ,  $-CH_2CH_2-$ ,  $-CH_2CH_2CH_2-$ ,  $-OCH_2-$ ,  $-CH_2O-$ ,  $-CH_2CH_2O-$ ,  $-OCH_2CH_2-$ ,  $-O-$ ,  $-N$ (lower alkyl)-,  $-N$ (lower alkyl) $CH_2-$ ,  $-CH_2N$ (lower alkyl)-,  $-S-$ ,  $-SO-$ ,  $-SO_2-$ ,  $-CH_2S-$ ,  $-SCH_2-$ ,  $-CH_2SO-$ ,  $-SOCH_2-$ ,  $-CH_2SO_2-$ , and  $-SO_2CH_2-$ ;

$R^5$  is H or  $C_1$ - $C_3$ -alkyl, with the proviso that both  $R^3$  and  $R^5$  cannot be alkyl;

$R^6$  is aryl;

$R^7$  is aryl or  $C_1$ - $C_3$ -alkylaryl;

$R^8$  is chosen from alkyl, aryl, heteroaryl, substituted alkyl,  $C_1$ - $C_4$ -alkylaryl,  $C_1$ -

C<sub>4</sub>-alkylheterocyclyl and C<sub>1</sub>-C<sub>4</sub>-alkylheteroaryl;

R<sup>9</sup> is chosen from H, alkyl, alkenyl, substituted alkyl, cycloalkyl, aryl, alkoxy, heteroaryl, fluoroalkyl, C<sub>1</sub>-C<sub>4</sub>-alkylcycloalkyl, (C<sub>1</sub>-C<sub>4</sub>-alkoxy)alkyl, (C<sub>1</sub>-C<sub>4</sub>-alkoxycarbonyl)alkyl, (C<sub>1</sub>-C<sub>4</sub>-alkylthio)alkyl, heterocyclyl, C<sub>1</sub>-C<sub>4</sub>-alkylheterocyclyl, C<sub>1</sub>-C<sub>4</sub>-alkylaryl, and C<sub>1</sub>-C<sub>4</sub>-alkylheteroaryl;

R<sup>10</sup> is H or C<sub>1</sub>-C<sub>3</sub>-alkyl, or

R<sup>9</sup> and R<sup>10</sup> taken together may form a 5- to 7-membered ring structure optionally containing O, S, SO, SO<sub>2</sub> or NR<sup>12</sup>, said ring optionally substituted with -OH, -CN, -COOH or -COOCH<sub>3</sub>;

R<sup>11</sup> is aryl;

R<sup>12</sup> is chosen from H, C<sub>1</sub>-C<sub>3</sub>-alkyl, alkoxycarbonyl, methoxyacetyl and aryl;

R<sup>13</sup> is chosen from -OH, -OTHP, 1-imidazolyl, and 1-pyrrolyl;

m is zero or one; and

n is zero or one, with the proviso that when A is A<sup>2</sup>, m and n cannot both be zero.